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GAS CHROMATOGRAPHY IN THE ANALYSIS OF SELECTED
CARDIO-PULMONARY PARAMETERS

by



BRIAN MALCOLM PETRIE

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE
OF MASTER OF ARTS

FACULTY OF PHYSICAL EDUCATION

EDMONTON, ALBERTA

JUNE, 1967

UNIVERSITY OF ALBERTA
FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "Gas Chromatography in the Analysis of Selected Cardio-Pulmonary Parameters," submitted by Brian Malcolm Petrie in partial fulfilment of the requirements for the degree of Master of Arts.

ABSTRACT

The purpose of this thesis was to discuss the procedures that should be adopted in developing the single-breath, breath-holding technique for the investigation of the pulmonary diffusing capacity of the lung for carbon monoxide and the pulmonary capillary blood flow.

In order to present a complete experimental design for this technique the development of the necessary apparatus was discussed and full plans made available so that the system may be readily duplicated.

Gas chromatography theory was discussed and related to the development of a satisfactory system for the analysis of the normal respiratory gases and the special gases introduced into the inspired mixtures for the investigation of the above parameters of pulmonary function.

A computer programme was developed to facilitate the rapid analysis of data and presented in a manner that is applicable to most of the computer systems in operation at this time. The programme, written in Fortran IV, enables the computation of up to seven trials for each subject and was specifically designed to be used in conjunction with the single-breath, breath-holding technique used for pulmonary function analysis.



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ACKNOWLEDGEMENTS

I am indebted to the members of my committee, Dr. R. B. J. Macnab, Dr. B. J. Sproule, Dr. M. L. Howell and Mr. R. G. Glassford for their guidance and assistance in the development of this thesis.

My thanks are also extended to Dr. P. N. Paez, whose counsel was invaluable throughout the conduct of the inquiry, particularly in the difficult early stages.

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CHAPTER I

STATEMENT OF THE PROBLEM

In the search for more effective ways to measure the parameters of fitness and the effects of training, physical education research is branching out into areas that have previously been associated with the field of medicine. The development of sophisticated apparatus and techniques has made it possible to investigate some of the determinants of fitness that previously had to be studied under operating room conditions or under close medical supervision.

One particular parameter that is of considerable interest is cardiac output, and measurements of this component of heart function has been restricted to the Direct Fick Technique involving catheterization (7,14,35), and the relatively inaccurate Foreign Gas Techniques (11,21).

Although the Foreign Gas methods have been modified to gain greater accuracy, the technique that seems to have the greatest future in the application to research problems of physical education, appears to be the single-breath, breath-holding technique for the study of the diffusing capacity of the lung for carbon monoxide and the determination of the pulmonary capillary blood flow (4,9,10,24,31). The latter application, using acetylene in the inspired gases, provides a result that may be regarded as being equivalent to cardiac output.

A necessary prerequisite for the use of this technique is a

satisfactory method of gas analysis, and it is the gas chromatograph that has come to be associated with the procedure.

Once the technique has been established and the efficiency and accuracy of the chromatograph has been determined, the researcher is faced with the problem of dealing with the complex formulae for the treatment of the data, and considerable time is required for these mathematical operations. As the time could be spent more profitably on additional experimentation, an equally important research tool that should be incorporated into this procedure, is a computer programme written to fit the research design.

In this study, the problems encountered in the construction of the apparatus for use with the single-breath technique, as well as the procedures involved in the application of gas chromatography to the analysis of respiratory gases, and the development of an appropriate computer programme, will all be discussed. In this manner, it is hoped to provide a complete experimental design that will be available for the researcher in the area of physiology of exercise.

The Problem

The purpose of this thesis then, is to discuss the procedures that should be adopted in developing the single-breath, breath-holding, technique for the determination of the diffusing capacity of the lung for carbon monoxide, and pulmonary capillary blood flow. Component parts of this problem include:

1. the development of the required apparatus,
2. the choice of an appropriate gas chromatograph, the selection

of appropriate columns to be used for the separation of the gas mixtures into measurable components, and the determination of the efficiency of the instrument, and

3. the development of a computer programme to facilitate the rapid analysis of data, and which would be sufficiently flexible to allow application to different computers and different research designs.

Sub-Problems

In order to understand the reasons behind the selection of particular components of a gas chromatograph system, and to assist in the selection of appropriate materials to be used for separation of the gas mixtures into their component parts, it is important that gas chromatograph theory be discussed.

An understanding of the experimental procedures that should be used in the determination of the diffusing capacity of the lung for carbon monoxide and the pulmonary capillary blood flow is required, and for this reason, both will be developed. This information is included, not only to assist in the application of these procedures to physical education research, but also to clarify the discussion of the development of the apparatus and the problems that are involved.

Limitations of the Study

A large body of literature exists in support of the theories of gas chromatography and pulmonary diffusion, and although both areas will be treated in this study, the discussion will be limited primarily to areas of relevance to respiratory gas analysis and to the two pulmonary

measurements of interest.

The discussion will be limited with respect to the fact that only one type of gas chromatograph was available for use in the development of the techniques under discussion. The principles of respiratory gas analysis by gas chromatography are, however, relatively basic and it may be expected that the procedures recommended are applicable, regardless of the make or model of chromatograph used.

Delimitations of the Study

The computer programme has been developed primarily for use with an IBM 7040 computer, and the language used is Fortran IV (1,27). Throughout the development of the programme, care has been taken to ensure that it can be used, with minor modifications, on any other computing system. There are, however, different procedures followed at various centres, particularly with regard to the Monitor System Cards, and the application of the programme to local conditions should be decided in consultation with the computer programmers.

The Importance of the Study

With the development of sophisticated instrumentation and complex experimental techniques for the measurement of parameters important to the assessment of fitness, it is essential that important advances are discussed and presented so that they may be applied as widely as possible throughout the field.

The single-breath, breath-holding technique is of particular importance as it allows the measurement of important parameters of cardiac

and pulmonary function. The measurement of the diffusing capacity of the lung for carbon monoxide permits a quantitative assessment to be made of the efficiency of gas diffusion from the alveoli of the lung across the membrane and into the blood stream, and permits investigation of the possible effects of training and conditioning upon the diffusing capacity. Measurement of the pulmonary capillary blood flow gives a close approximation of the cardiac output, and if the heart rate is determined simultaneously, stroke volume can also be determined.

The particular advantage of the technique is that measurements of these important parameters of pulmonary and cardiac function may be made without the close supervision of medical personnel.

Definition of Terms

Active Solid, a porous solid which is capable of separating the components of a sample without the addition of liquid coating. In this case, the action of the column is one of adsorption rather than solution.

Adsorption, the process of separation of a sample mixture into its component parts by means of the adhesion of the gas molecules to the surface of an active solid. These molecules may be released by heating.

Alveolar Volume (in milliliters), the volume of air inspired added to the residual volume of the lung. Alveolar volume represents the total volume of air from which diffusion occurred.

Alveoli; the terminal air sacs of the lung in which gas diffusion takes place.

Baseline, the portion of the chromatogram between peaks when no gas sample is being eluted. The baseline must coincide with the zero response from the detector.

Cardiac Index (in liters/minute/square meter of body surface area), the cardiac output expressed per unit of body surface area. It is a mathematical correction for the influence of varying body proportions upon the cardiac output.

Cardiac Output (in liters/minute), the blood flow from the left ventricle of the heart into the systemic circulation per minute.

Carrier Gas, the mobile phase in gas chromatography. The gas that is used to move the sample through the column.

Chromatogram, a plot of the detector response against the time of volume of the carrier gas. As this plot is usually accomplished with a recorder, the chromatogram is usually in the form of detector response against time.

Chromatography, an analytical method of separation based on the differences in the partition coefficients of substances distributed between a static phase and a moving phase.

Column, the part of the apparatus that accomplishes the separation of the sample components. It contains a packing material which consists of a solid phase, or a liquid phase on a solid support.

Column Efficiency, this is usually referred to in terms of the number of theoretical plates because of the similarity of a gas chromatographic column to a distillation column. In gas chromatography, the number of theoretical plates of a column can be obtained from the

chromatogram by relating retention volume or retention time, to the width of the peak as measured at the base.

Detector, the part of the gas chromatograph that measures a change in the composition of the effluent from the columns. It measures the amount of the sample component in the carrier gas as the carrier gas leaves the column and enters the detector.

Differential Detector, a detector that measures the instantaneous concentration of the gas being eluted from the column.

Diffusing Capacity of the Lung for Carbon Monoxide (in milliliters of gas/minute/millimeter of mercury), the capacity of the pulmonary membrane to transfer carbon monoxide from the alveoli into the blood stream.

Displacement Analysis, the process of analysis of a gas mixture that has been introduced into a column, together with a carrier gas that is more strongly adsorbed by the solid phase than any of the sample components. Thus, there is a competition for the static phase between the mobile phase and the component parts of the mixture. Consequently, the components are displaced along the column at different rates.

Elution Analysis, a sample of a mixture to be analysed is introduced into an inert carrier gas and carried through the column. Partition of the mixed substances occurs many times during the period that the sample remains in the column, and in consequence, separation of the components occurs.

Flow Rate, the volume flow rate of the carrier gas at the column outlet.

Frontal Analysis, a steady stream of the mixture to be analysed (whether diluted or not) is introduced into an inert carrier gas at a constant initial concentration. The components of the mixture are adsorbed by the fixed phase until an equilibrium is reached for each component, the moving front of the mobile phase being depleted of the mixture components in direct proportion to their partition coefficients. The result is that there is separation in the moving front and appearance of the components at the column outlet at different times. The column must be regenerated after each analysis.

Gas Chromatography, all chromatographic methods which use a gas as the mobile phase. A collective name for gas-liquid and gas-solid chromatography.

Gas-Liquid Chromatography, the technique of chromatography that uses a gas as the mobile phase and a liquid distributed on a solid support as the stationary phase.

Gas-Solid Chromatography, all chromatographic methods that use a gas as the mobile phase and an active solid as the stationary phase.

Height Equivalent to the Theoretical Plate, the length of column required for equilibrium to occur between the vapour in the gas and the vapour in the stationary phase.

Integral Detector, a detector that measures the accumulation of the sample.

Integrated Area, the area under the peak which is measured by an electrical or mechanical integrator.

Liquid Phase, a liquid which is essentially non-volatile at the operating temperatures of the column, and which is used to coat a solid

support and form the packing of a chromatograph column. The sample components are dissolved in the liquid as the sample moves through the column and the separation of the sample components depends on their differences in volatility in the solution.

Membrane Diffusion of the Lung (in milliliters of gas/minute/millimeter of mercury), the diffusing capacity of the whole lung membrane for carbon monoxide. Membrane diffusing capacity is a truer estimate of the diffusion of gas across the pulmonary membrane because it takes into account the plasma carbon monoxide pressure necessary to sustain movement of the gas into the red cell.

Partition Coefficient, the measure of the adsorption of a vapour on the adsorbant, which determines the speed of the zone of vapour through the column.

Peak, the recorded response of a differential detector to the presence of a sample component.

Pulmonary Capillary Blood Flow (in milliliters of blood/minute), the flow of blood through the pulmonary capillaries per minute, as measured by the diffusion of acetylene across the pulmonary membrane into the red blood cells.

Pulmonary Capillary Blood Volume (in milliliters), the volume of blood in the pulmonary capillary bed.

Resolution, the separation factor between peaks. When the back and front of adjacent peaks reach the baseline at the same point, they are properly resolved and have a calculated resolution factor of 1.5. Values less than this imply incomplete separation.

Retention Time, the time taken from the beginning of sample injection to the maximal height of a particular peak.

Retention Volume, the product of retention time and volumetric flow rate. The volume of carrier gas, measured at or corrected for the column temperature and column outlet pressure, which passes through the column between the time the sample is injected and the peak maximum occurs.

Sample Injector, a device for introducing a gas or liquid sample into the gas chromatograph. The sampling chamber has a certain volume which is not part of the column and this is termed the sample injector volume.

Solid Support, this consists usually of an inert porous solid such as a diatomaceous earth. The efficiency of the column is influenced by the particle size and surface area of the solid support.

Stroke Index, (in milliliters of blood/beat/square meter of body surface area), the amount of blood ejected from the left ventricle of the heart per beat corrected for body surface area variations.

Stroke Volume (in milliliters of blood/beat), the amount of blood expelled from the left ventricle of the heart by the end of each systolic period. In the present context, stroke volume is defined as the pulmonary capillary blood flow per minute, divided by the minute heart rate measured during the breath-holding period.

Theoretical Plate, the zone of a chromatographic column of sufficient length to allow complete equilibrium to take place between the vapour in the gas phase, and the vapour in the stationary phase.

Thermal Conductivity, the capacity of a gas to conduct heat. The thermal conductivity varies for different gases, being very high for helium and hydrogen and much less for the respiratory gases. The introduction of a gas of low thermal conductivity into a carrier gas such as helium will reduce its heat conductivity and will cause the detector cell to heat. An electrical current will be drawn across the galvanometer of the Wheatstone Bridge because of the change in resistance of the heated detector.

Tissue Volume (in milliliters), the volume of the pulmonary parenchymal tissue.

Wheatstone Bridge, an electrical circuit consisting of four resistors, each on a separate arm of the circuit. When the four resistors form the detector elements of a thermal conductivity cell, the current across the bridge through a galvanometer is balanced when pure carrier gas is flowing over all the detectors. When another gas is mixed with the carrier gas, the resistance of the detector exposed to this mixture is changed and the circuit becomes unbalanced. Additional current is then drawn by the heated detector through the galvanometer which registers the change in flow of the current.

CHAPTER II

GAS CHROMATOGRAPHY

Chromatography is a method of separating a mixture into its component parts by utilising the differences between the partition coefficients of the substances when they are distributed between two different materials. These materials are known as phases and one makes up the static phase, usually of a large surface area, and the other is a moving phase. The moving phase, which contains the mixture to be separated, passes through the static phase, and in the process, the component parts of the mixture are retarded by or attracted to the static phase and are separated from each other (34:1).

Although such separations are performed by nature, it was not until 1906 that the technique came to be used as a scientific tool. At that time the Russian biologist, Tswett (37,38), separated the components of plant pigments by passing them through columns of solid adsorbents and, as the separated pigments formed coloured rings, Tswett gave the process the name "chromatography." Modern applications have been far removed from colour separation, but, although the name now appears to be a misnomer, it has not been changed.

The use of a gas as the fluid phase was forecast by Martin and Synge in 1941 (26), when they showed that it was possible to separate substances on the basis of a liquid-liquid system. Their finding that paper strips could be substituted for columns was of particular significance for the development of chromatography as a research tool for

organic and bio-chemistry.

In that study it was suggested that a gas could be used in place of the flowing liquid, but it was not until 1952 that Martin, this time working in collaboration with James (15), was able to successfully demonstrate elution gas chromatography.

Since that time, the development of gas chromatography has been particularly rapid, and the technique has been applied to virtually all branches of analytical chemistry.

Gas Chromatography Theory

Generally speaking, all gas chromatographic systems operate the same way. The static phase is fixed and has a large surface area and may consist of a liquid held by a solid (partition chromatography), or it may be an active solid (adsorption chromatography). The static phase is usually contained in a column of stainless steel which may range from one-sixteenth of an inch to a quarter of an inch in outside diameter. The moving or mobile phase is a gas and always carries the sample to be analysed through the column containing packing material.

The mixture to be analysed is injected into the mobile phase which then carries it into the column containing the static phase. Some components may be swept through the column without being retarded, some may be completely adsorbed by the static phase, while others may undergo partition between the adsorbent and the carrier gas and be separated from the other components during passage along the column (16:6).

As the mobile phase passes from the column, it carries with it, first those gases that were not retarded, and then, in turn, the components

that were separated or fractionated during passage through the column. These gases, still carried in the mobile phase, are passed through a detector that is capable of measuring changes in status of the carrier gas due to its combination with the components of the mixture. Such changes are converted into electrical signals that may be recorded.

The major elements of a gas chromatographic system, then, include a carrier gas, a device for injecting a sample into the carrier gas flow, a column or columns containing suitable packing material to enable thorough separation of the components of the mixture, a thermostatically-controlled oven surrounding the column so that the temperature can be kept constant, a thermostatically-controlled and heated detector, and a sensitive strip chart recorder.

Carrier gas. The selection of an appropriate carrier gas must be made from among those gases that are not required for analysis, are not adsorbed by the column packing material and are not harmful to the detection system.

The type of detector system will also affect the choice of the carrier gas; the thermal conductivity detectors may use a wide variety of carrier gases, with hydrogen, helium, argon and nitrogen being preferred; gas-density balance detectors use argon or nitrogen; flame thermocouple detectors have hydrogen as the carrier gas, with an additional supply of oxygen to assist combustion; and the ionization detectors may use argon, helium, hydrogen, nitrogen, or a hydrogen-nitrogen mixture, depending upon the particular type of detector (16:38-71).

In all cases, it is advisable to adjust the flow of carrier gas

to the chromatograph by fitting a two-stage regulator to the gas cylinder, and, as some impurities may be present in the cylinder, a drying filter containing silica gel or molecular sieve should be fitted in the supply line. This drying column also helps to buffer the flow and assist in maintaining constancy (34:253).

For normal analyses, very close control over flow may not be necessary, with variations to the order of ± 1 per cent being tolerable, however, as sensitivity, analysis time and separation are all altered by changes in flow, it is essential that the flow for calibration analyses be the same as that for analysis of the sample mixture.

Flow is also controlled at the instrument itself, usually by a needle valve, and the passage of the carrier gas through the columns is adjusted by the introduction of restrictors. It is important to realize that very small changes in ambient temperature can lead to very large changes in the flow of carrier gas through each orifice of the control valves, and for this reason, it is advisable that the temperature of the carrier gas flow and that of the control valves be thermostatically controlled. Where automatic control of the analysis cycle is in use, rigid control over flow is imperative and all parts of the flow system should be equipped with thermostats (34:254).

The carrier gas flow through the columns must be checked frequently, preferably prior to each series of analyses. There are many ways to perform this measurement, and these include the use of a rotameter, a capillary manometer, an orifice meter or a soap bubble meter. Rotameters are only suitable for providing a rough indication of flow

and are not sufficiently accurate. The calibration of the capillary meters is difficult and fitting these devices into the system is also a problem. The soap bubble flow meter is the simplest system, and is also the most accurate. To construct one of these devices, a burette, calibrated in milliliters, is modified by replacing the stopcock with a hooked T-piece of glass. The hook is fitted with a rubber bulb filled with soap or detergent, and the other arm of the T is connected to the outlet from the detectors of the chromatograph. When the bulb is squeezed, a bubble is forced past the entrance port for the gas. The gas flow then pushes the bubble up the column of the burette and it is a simple matter to time the passage of the bubble past ten milliliters of graduations on the column and to convert the time to flow in milliliters/minute. Before measurement it is advisable to allow several bubbles to pass up the full length of the burette to moisten the sides.

When packing new columns, flow rates should be compared between the old and new columns, in order that the reproducibility of the packing technique can be determined.

Sample transfer methods. The aim is to inject the quantity of the sample into the carrier gas stream in a quantitative and reproducible manner, and to ensure that there is no contamination or interference with the carrier gas flow. As the sample should be injected so as to occupy a minimum of column length at the commencement of the analysis, the speed of injection is of particular importance, especially with flame methods, as an interruption in flow can extinguish the flame (16:8).

The sample introduced should be a gas, a liquid that can be vaporized in a heated injector, or a liquid or solid that will decompose under heat and give off gases.

There are various techniques for introducing samples into a gas chromatograph, these being:

- (a) direct injection into the carrier gas stream,
- (b) by the use of sampling valves,
- (c) by automatic or semi-automatic devices, or
- (d) by miscellaneous devices.

1. Direct injection. The sample to be analysed is drawn from a collection chamber into a gas-tight syringe. A hypodermic needle fitted to the syringe is then inserted through a rubber septum and the sample rapidly discharged into the carrier gas stream. Experimentation has shown that this technique is not suitable for quantitative and reproducible analysis as the length of time taken to empty the syringe varies and this will cause a variation in the column length occupied by the sample at the commencement of analysis. This method of sample introduction cannot be recommended where a high degree of accuracy is required, or where the determinations required include components that are present in major proportions (16:9).

2. Sampling valves. These consist of many types, and the system may use a constant volume pipette, four-way taps, multi-port valves or syringe injection into a sample loop. In all cases, the aim is to pass the sample into a by-pass loop of known volume, and to turn a tap that

will isolate the sample loop from the outside source and connect it to the carrier gas flow. With these devices, care should be taken to flush out all the air present in the loop with the sample before turning the tap.

The pipette systems have particular disadvantages, especially as it is difficult to construct leak-proof metal pipettes and the glass ones are prone to breakage. Although this type of sample injection system is simple and reproducible results can be obtained, their use is limited by: (a) the necessity of collecting large volumes of sample gas, to purge the pipette, (b) of having to turn at least three taps in order to introduce the sample into the system, (c) of requiring carefully prepared gas mixtures for detector calibration, and (d) needing volume calibrations to be made (16:10).

Four-way valves and multi-port sampling units are particularly effective if they are made from metal to satisfactory levels of precision. The difficulties of the need for pressure measurement and volume calibration remain. A design by Pratt and Purnell (33) consists of a barrel and shaft made of stainless steel. The shaft has six grooves each of which contain a silicone rubber O-ring. Four of these grooves are sloped along the shaft to produce four on-off valves which allow the gas to pass from one port to another through the space between the O-rings. This type of valve is fitted to several commercially produced chromatographs, and has been found to perform satisfactorily provided the pressure generated by forcing the sample into the sample loop is allowed to equilibrate with the atmosphere before turning the tap.

Syringe injection into a sample loop has the advantage of providing the simplicity and ease of operation of syringe injection, coupled with the advantage of permitting a constant volume to be injected into a loop kept at atmospheric pressure. Certain difficulties remain, particularly with regard to the problem of operator technique, as the injection must be performed in exactly the same way each time, if reproducible results are to be obtained (16:12).

3. Automatic and semi-automatic sampling devices. Metal multi-port, constant volume sampling valves have been designed to be operated mechanically or pneumatically. These devices reduce many of the errors that occur in sampling, but care should be taken to periodically check for leaks.

One such valve has been described by Peterson and Lundberg (32) who made a valve so that the sample could be introduced through a hole in a shaft which could be moved between two chambers. The sample gas passed through one of the chambers, and the carrier gas through the other. After sufficient time was allowed to enable the sample chamber to be purged, a pneumatic device lifted the shaft so that the sample contained in the hole in the shaft was lifted into the carrier gas chamber. The sample was then swept from the hole by the carrier gas and into the column. The size of the sample in this system is adjusted by varying the size of the hole in the shaft.

Other methods are in use that are similar to that described by Pratt and Purnell (33), except that the grooves on the shaft are not sloped. The sample is passed into the barrel and flows around a chamber formed by the placement of two O-rings. Carrier gas flows through

similar chambers. When the sample is to be passed into the column, compressed air slides the shaft along the barrel and the sample is swept from its chamber by the carrier gas.

4. Miscellaneous methods. Various techniques have been devised for injecting particular substances into gas chromatographs. As those sampling systems are not meant for general use, it is sufficient to say that they are mainly used with minute quantities of the sample, or with substances that are difficult to inject with conventional systems.

Column performance and chromatographic separation. These factors will be discussed under separate headings.

1. Column performance. The speed of movement of a component through a column is governed partly by the ease of adsorption of the vapour, which in the case of gas-liquid chromatography is measured by the partition coefficient. The speed of movement of the zone of vapour through the column determines the total time that the zone will take to pass completely through from one end of the column to the other. This time taken to traverse the column is known as the retention time. Although the retention time is a function of many factors, a major influence is the flow rate of the carrier gas. The greater the flow rate, the shorter will be the retention time, and the retention time and flow rate are inversely proportional so long as the pressure drop across the column is small. The constant product of the flow rate and the retention time is equal to the amount of carrier gas required to move the zone of vapour from one end of the column to the other. This

column component is known as the retention volume (25:8).

A chromatogram may be used to determine if a gas sample is pure, to enable the identification of the component parts of a gas mixture by the comparison of retention times of the unknown peaks with retention times of known components, or, more frequently, for quantitative analysis of known mixtures. The chromatogram may also be used for determining the efficiency of the chromatograph itself.

If adequate measurement is to be made, the chromatograph must be capable of separating the components from each other, and it is possible that some gases may have similar retention times for the particular operating conditions of the chromatograph and their peaks might overlap. These overlaps may be caused by either of two situations, closeness of the peaks, or width of the bases of the peaks, both of which are largely independent. The closeness of the two peaks is due to the similarity of their retention volumes and may be remedied by using a more suitable stationary phase. The peak width is due to deficiencies in column performance. Separation may be greatly improved by increasing the relative retention (the ratio of the retention volumes of the two components) and by improving the column performance. The factors that influence the retention volume include the column variables of dead volume, pressure drop across the column, temperature of the carrier gas as it affects the flow rate and the weight of the stationary phase, the thermodynamic factors of the chemical nature of the vapour, the chemical nature of the stationary phase and the temperature of the column as it affects the thermodynamics (25:30).

Column performance is evaluated in terms of the Plate Theory of Martin and Synge (26). In order to understand this concept, it is best to visualise the chromatographic column as being divided along its length into a number of separate zones, each of these zones being of sufficient length to allow equilibrium of the vapour to take place in the gas and stationary phases. Each of these zones is called a Theoretical Plate, and the length of each plate is known as the Height Equivalent to the Theoretical Plate, or HETP.

At the beginning of the analysis, the vapour is completely contained within the first plate. When an incremental volume of carrier gas is passed into the column, some of the vapour in the gas phase is forced into the next plate where it equilibrates with the stationary phase, while that remaining in the stationary phase and carrier gas at the first plate equilibrates with the clean carrier gas that flows into it. The process continues as more carrier gas enters the column, and slowly the loading section of the vapour moves along the column while the concentration of vapour in the first plate diminishes until none remains. The way in which the vapour is distributed among the plates after a passage of a number of carrier gas increments is dependent upon the amount of vapour that is transferred at each incremental passage (25:120). The HETP is related to the cross-section area of the column occupied by the gas phase, the cross-section area of the column occupied by the stationary phase, the partition coefficient of the solute, the concentration of the vapour in the gas phase and the incremental volume of the carrier gas.

The number of theoretical plates can be calculated from the

chromatogram by using the equation (36):

$$N = 16(d/w)^2$$

where:

n = the number of theoretical plates,

d = the distance from the point of injection of the sample
to the highest point of the peak along the baseline,

w = the width of the peak at the baseline.

Once the number of theoretical plates is known, the determination of the HETP can be made using the equation (36):

$$\text{HETP} = L/n$$

where:

HETP = the height equivalent to the theoretical plate,

L = the length of the column,

n = the number of theoretical plates.

The number of theoretical plates varies with certain operating conditions such as carrier gas flow rate, column length and temperature. A column has a maximal value of n over a limited range of flow rates and the optimum flow rate for that column can be determined by plotting a graph with linear gas flow velocity as the independent variable, against HETP.

When the HETP is a minimum, then the column will contain the maximal number of theoretical plates, and thus, this would be the maximal expression of column efficiency. The optimal carrier gas flow rate would correspond to the minimum HETP and should produce an air pack in three-four seconds per foot of column (36).

2. Chromatographic separation. The majority of separations in gas chromatography use liquid stationary phases that have been dispersed upon inert supporting substances. In these cases, the resulting peaks are symmetrical in shape and are regarded as being almost the ideal type of chromatogram.

Where separation of gaseous mixtures is required, solid adsorbents are frequently used, and the resultant peaks tend to be sharp at the front, but tail off to a certain extent to the rear of the peak. For this type of peak, the response calibration is seldom linear, and often a correction factor must be established by repeated determinations using accurately prepared dilutions of each of the gases that are important to the study contemplated (16:23).

Only a small number of materials are used for packing columns in gas-solid chromatography, and these include silica gel, activated charcoal, alumina and molecular sieves. These materials are packed into columns that may be glass, brass, copper, aluminium or stainless steel. Stainless steel is preferred as it is non-corrosive and easy to bend. Columns should be fitted into the chromatograph using Swagelok, Burton, Simplifix or Tecalimit fittings as they provide gas-tight seals at all connections.

The stationary phase is carefully prepared and passed through sieves so that the particle size will be as uniform as possible. The mesh size of the packing is of importance as the finer the mesh, the more restriction there will be to flow. The bottom end of the column to be packed is plugged with glass wool, and the packing material is poured into the top of the column. It is more convenient to fill the

column before bending it to fit into the chromatograph oven. In order to ensure evenness of packing density, a vibrator should be used as the material is poured into the column. This may be a small electric motor with a flat surface at the end of the shaft, or an engraving tool. When the spindle of the vibrator is held against the column, the material packs down fairly rapidly to the even porous structure required. Further vibration will pack the column tighter to a higher density and will increase the pressure drop across the column when it is installed, with a resultant decrease in column efficiency. When the column has been packed to satisfaction, the top is plugged with glass wool. In order to assist in the preparation of columns with reproducible column packing densities, the volume of the packing material used should be determined and recorded. This may be done by using a measuring cylinder as a container for the packing material while filling the column, and observing the volume used.

The column is then coiled to fit the chromatograph, care being taken to avoid forming air bubbles, by coiling to as large a diameter as possible. The minimum diameter of the coils should be ten centimeters (16:25).

The packing procedure is similar when gas-liquid columns are prepared. A necessary stage prior to the packing is coating of the inert solid (celite or firebrick being commonly used as supports), with the selected liquid phase. This dispersion is achieved by dissolving the liquid phase into a solvent such as acetone or methanol, and stirring the support substance into the mixture. The combination of the support, liquid phase and solvent is stirred continuously while evaporation takes

place. When the solvent has all evaporated and the material is apparently dry and free running, it is re-sieved and packed into the column (36).

Following packing, columns should be activated or conditioned, and this process involves placing the column into the chromatograph and increasing the temperature to between 200°C – 400°C . (depending upon the type of packing material) and leaving the column at that temperature for more than two hours.

It should be emphasised that while conditioning is being performed, the column outlet should be disconnected from the chromatograph as the packing material gives off a vapour that may damage the thermal conductivity detectors.

Column heating. For normal routine analyses, close control over temperatures may not be necessary, and constancy of temperature between $\pm 1^{\circ}\text{C}$. may be satisfactory. It is possible to make some analyses at ambient temperatures and, while a 1°C . change in column temperature may alter the retention volumes of substances by five per cent, all components will be more or less equally affected. Whether this approach can be employed or not depends upon the characteristics of the detector, and as certain detectors are responsive to changes in the retention volume, especially if peak height calibrations are employed, it is usually worthwhile to use a thermostatically-controlled column chamber or oven (34:256).

Although vapour baths and liquid baths have been used in attempts to provide a close control over the column temperature, a much better approach is to use an insulated metal box as a column container and to

circulate air through it with a fan. Most of the commercially produced units use this system, and fit the box or oven with a door so as to permit easy access to the columns. If this design is to operate satisfactorily, and provide an even distribution of temperature throughout the oven, the blower must be capable of providing a forced circulation of air with sufficient power to achieve linear velocities of above thirty-five feet per second, at which speed flow becomes turbulent at ordinary temperatures and pressures (34:257).

When analysing a mixture in a column at a constant temperature, the first peaks to be eluted are very high and narrow, while, if retention times are great, the last peaks will be wide and shallow. There is also a possibility that the measurement of the peaks will give erroneous quantitative values, whether this is due to the difficulty in measuring the area of the spread peaks, non-linearity of the detector to large concentrations or to the incorporation of excessive detector noise into the peak. In such cases, the problems can be eliminated by increasing the temperature of the column during the course of the analysis, so that the initial temperature is sufficient to produce reasonable shapes for the initial peaks, and the final temperature is high enough to allow the elution of the last peaks within a reasonable time. This change in temperature can be achieved in either of three ways (34:219-221):

(a) by discontinuous heating, either with or without an interruption in the carrier gas flow. The column is heated between the appearance of the volatile and less volatile components of the mixture,

(b) by uncontrolled continuous heating. The detector is kept at

a temperature greater than that of the column at its hottest, and the column is heated continuously from the time of the injection of the sample. Great care must be taken to ensure that the increase in temperature is linear,

(c) by linear temperature programming. In this technique, the column is heated with a linear relation between temperature and time. The advantage of this system is that the column is heated at a reproducible rate.

Detectors. The function of a detector is to record the presence of a component of the gas mixture being analysed and to indicate the quantity of the substance present or the concentration of the component. Although there is a wide variety of detectors available, each making use of chemical or physical properties in their sensing mechanism, those that are more widely used provide an electrical signal that can be amplified for recording purposes.

The detectors used in gas chromatography may belong to two categories (16:39):

(a) integral detectors where the response is a function of the total quantity of the material such as the sample gas that has passed through the detector, and

(b) differential detectors where the response is a function of the gas concentration at any particular time.

The integral detectors have particular disadvantages that limit their general applicability. These disadvantages include a lack of sensitivity and the problem that the component gases may be re-combined within the detector chamber, unless special steps are taken for their

isolation (16:39).

Differential detectors are particularly numerous and no attempt will be made here to fully describe the operation of each. Instead, as the Thermal Conductivity Cell (Katharometer) has the greatest application to respiratory gas analysis, it will be discussed in detail, and only the general principles underlying the others will be treated.

1. The thermal conductivity cell. Shakespear patented a device, which he called a Katharometer, in 1915 (34:278) and this instrument was the forerunner of the instruments in use today. The modern version consists of aluminium chamber, the walls of which are held at a constant temperature. Within the chamber, is an electrically-heated hot element of metal or semi-conductive material. A stream of carrier gas passes through the chamber or past it (gas flowing into it in this case by diffusion) and any component of the sample mixture will be carried by the carrier gas to the chamber. When pure carrier gas is flowing through the system, and there is a constant current to the hot element, the rate of heat production is constant and the heat is dissipated by conduction through the gas. The presence of a vapour of a component ". . . changes the thermal conductivity of the (carrier) gas, so that a different temperature gradient is necessary to maintain the required rate of dissipation, and therefore the hot element changes temperature" (25:302).

The temperature of the hot element is measured as if it were a resistance thermometer, with a change in temperature producing a change in resistance. This change in resistance may be measured by using the hot element as one arm of a Wheatstone Bridge. If two thermal

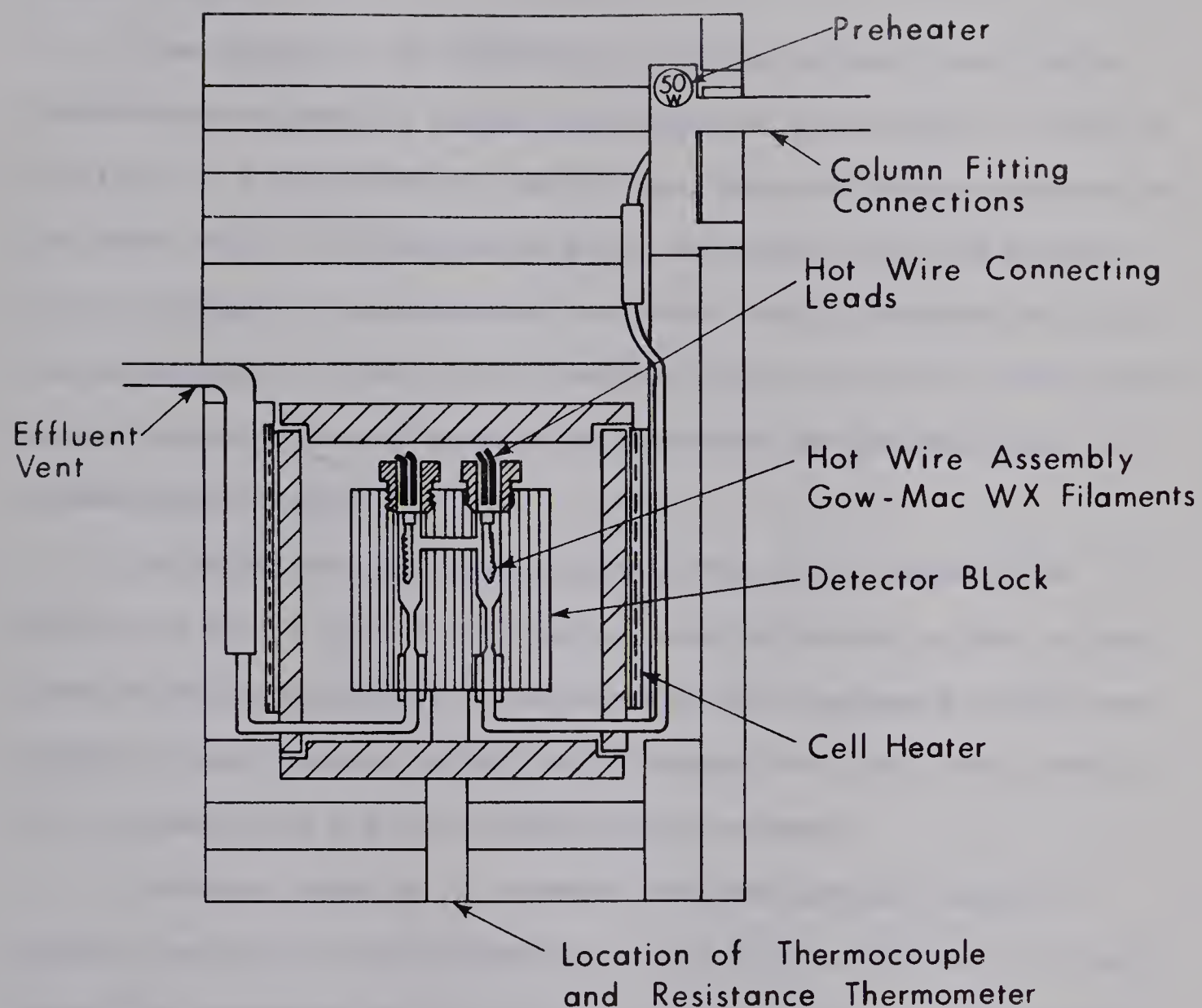


FIGURE 1 THERMAL CONDUCTIVITY DETECTOR ASSEMBLY
GOW-MAC FILAMENTS MICROTEK GC2013M GAS
CHROMATOGRAPH (28)

conductivity cells are placed to form adjacent arms of a Wheatstone Bridge, one to measure the output from the columns and one to continually measure pure carrier gas, instrumental drift can be greatly reduced (25:303).

The changes in the resistance of the hot element result in an out-of-balance potential across the Wheatstone Bridge which can then be displayed on a galvanometer. As the resistances of the hot elements and the other arms of the Wheatstone Bridge are smaller than the maximal input impedance of potentiometric recorders, such a recorder may replace the galvanometer in the circuit, and the continuous record of the out-of-balance electromagnetic force of the Wheatstone Bridge would form the chromatogram (25:303).

An attenuator may also be added to the circuit between the Wheatstone Bridge and the recorder to allow the maximal signal to pass from the Wheatstone Bridge to the recorder for measurement of gas components of small concentration, and to reduce the signal where gases of high concentration are being detected and analysed.

Different types of hot elements are used and care should be taken to ensure that the temperature of the walls of the cell are kept below the recommended maximum for that type of detector. The maximal temperature for thermister type thermal conductivity elements is about 100°C. The manufacturer's specifications will show the optimal temperature for maximal sensitivity.

When working with mixtures containing high concentrations of oxygen, some of the detectors begin to lose efficiency through oxidation, and this may be detected by seeing if the oxygen peak returns to

the previously established baseline after analysis of the gas.

Some of the more modern types of thermal conductivity detector cells use four hot elements. Two are placed in the pure carrier gas stream and the other two are used for detecting component gases mixed with the carrier gas. In this manner, the sensitivity of the thermal conductivity cell may be doubled (34:281).

2. Gas-density balance detectors. This technique employs comparison of gaseous densities for molecular weight or composition measurement. The apparatus, as developed by Claesson (6), consisted of a liquid manometer connected across two columns of gas, one of which contained pure reference gas. Any difference in mass between the two columns due to the presence of the component of a sample, set up a pressure differential which was measurable in direct proportion to the differences in mass. Martin and James miniaturised the system and were able to convert the pressure differential into a strong electrical signal (34).

In a more recent development, Gow-Mac Instrument Company, under license from the Standard Oil Company of Indiana, simplified the apparatus for commercial development.

This detector is in the form of a metal block with several internal flow passages. In two of these passages are sensing elements that are connected to the external resistors of a Wheatstone Bridge circuit. A thermal imbalance of the Wheatstone Bridge is created by changes in the flow of the carrier gas over the sensing elements (16:49). In Figure 2, the pure carrier gas enters the block at E and gas from the

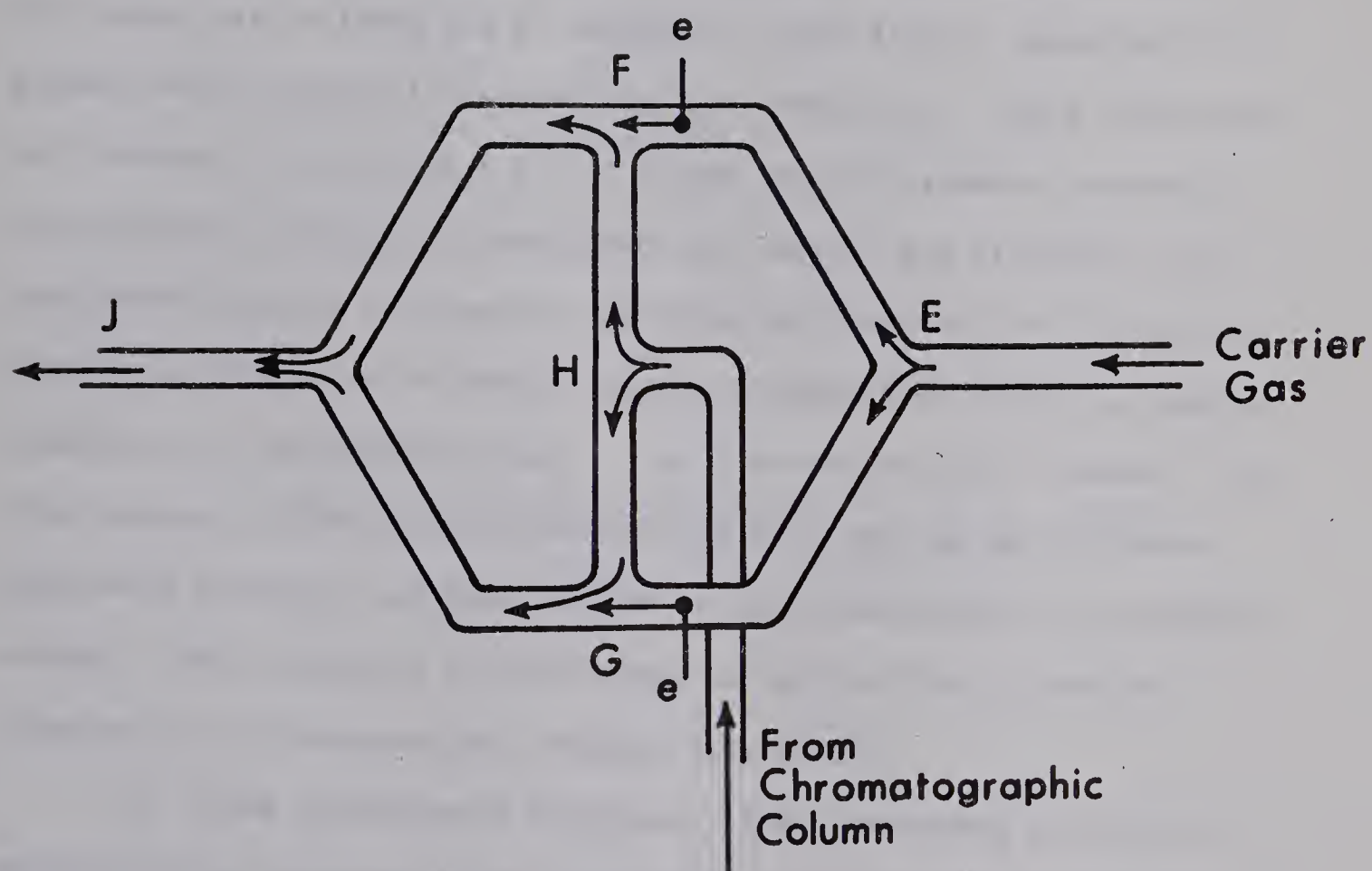


FIGURE 2 GAS-DENSITY BALANCE DETECTOR. FROM JEFFERY AND KIPPING (16:50)

chromatograph column enters at H. When pure carrier gas enters from both ports, the flow from E divides equally and flows into the passages EF and EG before passing from the balance at J. When a gas of a higher specific gravity than the carrier gas enters the system at H, where the flow is less than that at E, the equal division of the pure carrier gas into the tubes EF and EG is disturbed because of the density gradient that has been set up in the vertical column FG. This causes more of the sample gas to leave the FG column at G than from F, resulting in a proportional increase in carrier gas flow from E to F, and a corresponding decrease in flow from E to G. As the sensing elements located in the positions labelled "e" are within the carrier gas flow only, any unbalanced increase in flow will increase the resistance of one of the hot-wire or thermister elements, and, as it will also receive a smaller proportion of the Bridge current, it will be cooled still further. The other element in the area of reduced flow will heat up and its resistance will decrease, and thus receive an increased supply of the Bridge current. This imbalance in the thermal conductivity will then be recorded as the chromatograph response (16:49-52).

3. Flame thermocouple detectors. These detectors are mostly applied to the analysis of the hydrocarbon gases and the technique of analysis involves the burning of hydrogen, either as carrier gas or as an introduced gas, within the detector chamber. The flame is adjusted so that its peak is just below the hot junction of a thermocouple when pure carrier gas is flowing through the detector. When sample gases are present, the organic substances present burn within the flame, causing

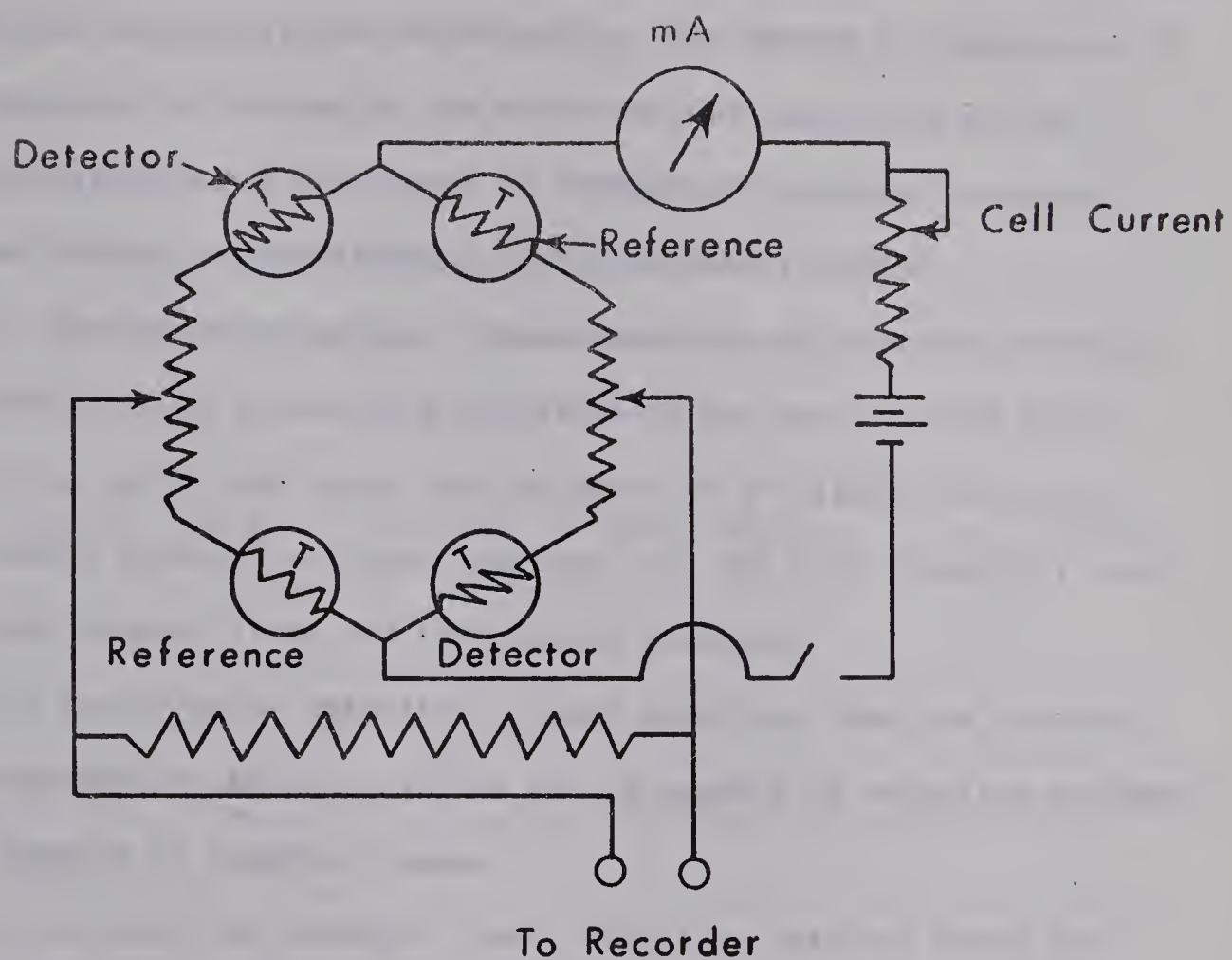


FIGURE 3 WHEATSTONE BRIDGE CIRCUIT, AFTER
HAMILTON, ET AL. (13:7)

it to enlarge and engulf the thermocouple. The change in temperature of the thermocouple is related to the molar heat of combustion of the components present, and the change in temperature produces a current that flows through a potentiometer to be recorded (16:53).

4. Ionization detectors. These detectors all use the principle of the conduction of electricity by gas which has been ionized by an energy source and placed under the influence of an electrical field. Various energy sources have been employed, but the more frequently used sources are hydrogen flame and radioactive isotopes.

This technique of detection is more sensitive than the Katharometer or gas-density balance systems and is capable of detecting extremely small samples of component gases.

In practice, the hydrogen flame ionization detector burns its carrier gas in a hydrogen flame, and these gases become hot enough for a small proportion of the molecules to acquire sufficient energy to ionize and give the flame an electrical conductivity. When an organic vapour enters the flame, the conductivity is increased and it is this increase that is measured and recorded (25:288-89).

The argon cell ionization detector is very sensitive to organic materials but is insensitive to some of the hydrocarbons and the permanent gases. The argon carrier gas is exposed to ionizing radiation from a source such as strontium-90, radium-D, promethium-147 or tritium. With this irradiation, positive ions and free electrons are produced and it is these electrons, collected under the influence of the applied field, that give rise to the small electrical current that is the

standing current of the detector cell. Some of the argon molecules become excited by the radiation and the energy stored in these molecules is sufficient to cause ionization of the molecules of the sample components as they enter the detector chamber. These additional ions are collected by the anode and cause an increase in current through the cell that makes up the detector response (16:60).

Recorders and the measurement of chromatograms. A great variety of satisfactory recorders are commercially available. The prime characteristic for a suitable recorder is a rapid response time, and a full scale deflection from an input of one millivolt. It is a definite advantage if the recorder is fitted with an automatic integrator that measures the area under each peak as it is produced. Digital read-out integrators are also commercially available.

1. Peak identification. Frequently in gas chromatography, the isolation of the components of a sample mixture constitutes the easiest part of the analysis, as identification can be particularly difficult, especially when high sensitivity detectors indicate the presence of unsuspected small concentrations of unknown components in mixtures under analysis.

When the chromatographic technique is replacing a method that was well established, the components are known, and it is a simple matter to use individual reference gases of these components to detect the retention time of each (provided they are available).

When the chromatographic technique is the only one available, there are two possibilities. First, if the material to be analysed derives

from a known chemical reaction, then the components that result are predictable and their elution times can be determined as before. If, however, the mixtures to be analysed derive from natural or unknown sources, the identification of the components is particularly difficult. Often it is possible to use mass spectrometry, ultra-violet or infra-red spectrometry for identification of components as they elute from the detector outlet. Chemical analyses may be performed on the unknown mixture before chromatography.

It is possible to compare the retention times of the unknown peaks with those obtained under identical conditions for a wide range of materials. This method makes use of tables of relative retention data that may be found in the literature, but frequently, only provides a list of possible components with the same retention times. Retention times tend to be rather specific to the particular instrument and its operating conditions and the list of possible components would thus have to be broadened to include others with similar retention times.

Other identifications can be made by comparison of retention data of unknown components with those for standard substances plotted in the form of a semi-logarithmic plot with the log retention time or volume relative to a particular standard, against the boiling point or the number of structural units in the molecules of members of a particular series. This method is commonly used when pure samples of the full range of possible components are not available (34:388-89).

2. Quantitative analysis. Although other methods are used, the simplest and most frequently used technique for peak measurement uses

peak height or peak area for calibration purposes. These particular responses are the result of differential detector outputs and the displacement of the peak from the baseline records the concentration of the component in the detector at that time.

Peak height and peak area sensitivity are affected by column temperature, carrier gas flow rate, sample size, the type and concentration of the components and by the degree of resolution between the sample components.

The relative area sensitivity of the gas chromatograph does not change with a change in carrier gas flow rate, but individual component sensitivity varies inversely with flow. Therefore, if peak heights are used, calibration gases and samples must be analysed at the same carrier gas flow rate.

Column temperature does not affect the relative area sensitivity and has little effect on the individual component area sensitivity, provided a constant carrier gas flow rate is maintained as the temperature increases. Both relative peak height and component peak height sensitivity will change with temperature and it is therefore necessary to run the calibration and sample analyses under the same temperature conditions (36).

The measurement of peak height is more rapid and probably more accurate than measuring peak area. For this reason, it is usually preferred, although, if the sample size varies, the plots of peak height against sample size are often non-linear, and plots of peak area are more accurate under these situations. The reason behind this is that the theoretical plate heights, and thus the peak heights and widths, are

dependent upon sample size and sample feed volume, whereas the area under the peak is not. It is essential then, that all variables that may affect the HETP should be rigorously controlled if satisfactory results are to be obtained from the peak height method (34:399).

When a chromatograph is used that is fitted with automatic constant volume sampling injection and thermostated control of column temperature and carrier gas flow, the most satisfactory method to use for calibration is the measurement of peak height.

In assessing peak height, the measurement should be made from the maximal height of the peak, to a point directly below, on a baseline drawn between the point where the peak commenced to rise to where the baseline was reestablished. Often a peak does not return to the previously established base because of a decrease in the efficiency of the detector.

If peak area is used for calibration, there are often difficulties with asymmetric peaks, and Krejci and Janak (20) list, in increasing order of accuracy, the following methods that may be used to measure area:

- (a) cutting out and weighing the chromatograms,
- (b) counting the squares,
- (c) approximation of the curve to a triangle drawn through the inflexion points and calculated by the equation (base width multiplied by peak height/2) or from multiplying the height by the width of the peak at half the height, and by
- (d) planimetry.

A further accurate method involves the use of an automatic integrator which gives a written recording, in integrator units, of the area under each peak.

To determine the concentration of a gas from the knowledge of the chromatogram response (peak height or area) of the component of the unknown concentration, and the concentration and chromatogram response of a reference sample of the same gas (analysed under the same conditions), the following equation may be used:

$$C_{Uk.} = C_{R.} \times PR_{Uk.} / PR_{R.}$$

where,

C. = concentration in percent,

Uk. = gas of unknown concentration,

R = reference sample of same gas,

PR = chromatograph response in peak height or area.

Where two peaks overlap, it is satisfactory to measure the peak height of each to the established baseline, even where there is a difference in the magnitude of the size of the two peaks. Peak areas may also be measured with accuracy by either dropping a perpendicular from the saddle between the two peaks, or extrapolating the unresolved portions of the peaks to the baseline (34:400).

CHAPTER III

GAS CHROMATOGRAPHY AND RESPIRATORY GAS ANALYSIS

Apart from the common room air gases of oxygen, nitrogen, and carbon dioxide, various other gases including carbon monoxide, acetylene, helium, neon and nitrous oxide have been used to assist in the measurement of various parameters of respiratory and circulatory function.

There is no single chromatographic material that is capable of separating all these gases, so any system used for pulmonary research must use a two- or three-column chromatograph to achieve satisfactory separation of the components. By employing column switching valves between the columns, it is possible to make the analysis of the gases using only one detector.

Column Packing Materials

Silica gel. The ability of a column packed with silica gel to perform a separation will depend upon the method employed in its preparation, and for this reason, it is difficult to duplicate retention times from one column to another.

Silica gel is an active solid packing material and it is available in a size and quality range suitable for gas chromatography, with mesh sizes ranging from 40 to 200. This bulk material must be sized by sieving to the particular mesh range suitable for the analysis of the components before packing it into a column, the preferred mesh size for an one-eighth inch (outside diameter) column being 60/80.

After packing, the column must be activated (conditioned), and this is done by drying the column in a vacuum at a temperature of about 150°C . or drying it in room air at a temperature of between 200°C . and 300°C . (16:27). The column may be conditioned in position in the chromatograph, provided the column outlet is not connected to the detector, as the exhaust may damage the efficiency of the detector elements.

It is particularly important that any water vapour in the respiratory gases be removed before allowing the sample to enter the chromatograph, where water can reduce the efficiency of the silica gel column. This reduction in efficiency can be remedied by re-conditioning the column, using the same procedures as before.

Silica gel columns are used for the separation of such gases as acetylene, carbon dioxide and nitrous oxide. As acetylene tends to react with copper and brass to form an explosive mixture, the use of stainless steel columns and tubing throughout the areas of the chromatograph liable to be in contact with this gas, is recommended (16:120).

Molecular sieve. This is a trade name for a number of commercially produced, artificial zeolites, and it is usually obtained in the form of pellets that must be ground down to the required mesh sizes.

There are three types of molecular sieves, 4A which is sodium aluminium silicate, 5A calcium aluminium silicate and 13X or sodium aluminium silicate. The effective pore diameters of each are 4 Å, 5 Å and 10 Å, respectively. The molecular sieve that has the widest application in respiratory gas analysis is 5A (16:30).

Following sizing and packing, the molecular sieve may be activated

by heating to between 350° and 400°C . for two hours, and this may be done with the column in position but disconnected from the detector. Also, as the molecular sieve column is conditioned at a higher temperature than the silica gel column, a short, dummy column containing no packing material should be used in place of the silica gel column during initial and periodic conditioning so that carrier gas may still flow through the molecular sieve column. The molecular sieve column is also affected by water vapour and will gradually lose efficiency if satisfactory absorbent material is not used to eliminate it from the samples. Carbon dioxide is adsorbed completely by molecular sieve and it may be removed from the column together with the water vapour, by periodic conditioning. The gradual deterioration of the column will be observed as a progressive loss of the ability to separate oxygen and nitrogen.

Molecular sieves are used to separate neon, helium, oxygen, nitrogen and carbon monoxide.

For a given sample volume, the critical separation of a molecular sieve increases with an increase in column diameter, with one-quarter inch (outside diameter), columns being generally preferred. This increase in column diameter also has an undesirable effect of reducing the sensitivity to carbon monoxide, but this can be regained if the flow rate is reduced. This results in carbon monoxide remaining in the column a longer time, which may result in excessive broadening, so the best compromise appears to be a carrier gas flow rate of approximately 200 centimeters/second, which is equivalent to a pressure drop of approximately eleven pounds per square inch across a six foot column

packed with -52/+72 mesh molecular sieve (16).

The ability of molecular sieves to separate oxygen and nitrogen diminishes as the temperature of the column increases above that of room air. As acetylene is usually the gas with the longest retention time in the silica gel column, it is best to experiment to find the most satisfactory combination of carrier gas flow rate and temperature to allow for the complete separation of oxygen and nitrogen, and a convenient retention time for acetylene without drastically altering column efficiency. Also, as carbon dioxide and acetylene are completely adsorbed in the molecular sieve column, it is best to have the sample containing neon, oxygen, nitrogen, carbon dioxide, carbon monoxide and acetylene to pass through the silica gel column first. The flow should be shunted by the column switching valve to enable the two columns to work with the flows parallel rather than in series after the neon, oxygen, and nitrogen have eluted so that the carbon dioxide and acetylene will not be able to enter the molecular sieve column, but will pass directly from the silica gel column to the detector.

Other packing materials. Hamilton and Kory (12) used Ootol-S³ (di-2-ethyl hexyl sebacate) on an inert solid support to separate carbon dioxide and allow a carbon dioxide-free composite to pass on to a 13X molecular sieve column. The only gases separated for analysis in this case were oxygen, nitrogen and carbon dioxide.

In a later application, Hamilton, et al. (13), used hexamethylphosphoramide (HMPA) as a liquid phase on an inert solid support to analyse the standard respiratory gases.

Despite the experiments with other materials, most researchers appear to prefer the combination of silica gel and molecular sieve columns for their respiratory gas analyses.

Carrier Gas

Helium is usually preferred as a carrier gas as its thermal conductivity differs considerably from those of the respiratory gases, thus providing large changes in thermal conductivity as each component is measured (12:830). Helium is generally used in the determination of the residual volume of the lung, but this function may be taken over by any gas that is inert in lung tissue and does not pass into the blood stream, and neon is generally substituted for this purpose.

A molecular sieve filter should be installed in the carrier gas line close to the two-stage regulator, so that any impurities or water vapour may be removed from the gas before it enters the chromatograph.

Chromatograph Operation at the University of Alberta

The gas chromatograph used at the Fitness Research Unit of the Faculty of Physical Education of the University of Alberta for research into pulmonary function is a Microtek GC2013M automatic operation unit.

The columns used are:

(a) Silica Gel, 60/80 mesh, 6 feet x 1/8" outside diameter stainless steel,

(b) Molecular Sieve, 60/80 mesh, 8 feet x 1/8" outside diameter stainless steel, and

(c) Molecular Sieve, 80/100 mesh, 3 feet x 1/8" outside diameter stainless steel.

The chromatograph section of the system is a standard isothermal unit with a four element thermal conductivity cell using Gow-Mac WX hot-wire filaments. A heated valve oven contains a seven port pneumatically operated sampling valve and an eleven port pneumatically operated column switching valve. The analytical columns are mounted in an oven that is thermostatically controlled by a fully proportional temperature controller.

A separate module is fitted to provide for automatically controlled time programming and this unit consists of an automatic function selector and a digital time programmer. The digital time programmer is the major component, determining the complete sequence of all events. The programmer is designed to operate one sampling valve, up to two column switching valves, up to six independent range functions (one for each gas analysed), and a reset mechanism.

The automatic function selector receives time sequenced circuit closures from the programmer and uses them to provide for the required action. The relays which operate the sample and column switching valves, the automatic zero, the stepping switch which selects the ranges, and the range potentiometers (which act as a separate attenuator for each range) are located in this module (29:1-2).

The automatic zero is a serve-actuated, null balancing potentiometer which adds a voltage of equal magnitude and opposite polarity to the error signal coming from the detector bridge. Six switches are provided to allow zeroing between any of the peaks after the range signal is switched off. The automatic zero is not operated while a

range switch is on (29).

The automatic function selector provides a separate potentiometer for each range, and this feature allows each peak to be adjusted to the required size for convenience of measurement.

With this particular design, the carrier gas passes from the two-stage regulator, into a 5A molecular sieve filter-drier, and from there to the pressure gauge in the instrument itself. From there, the carrier gas flow splits into two separate streams, one stream passing through the left hand rotameter, through the gas sampling valve and into column #1 (silica gel). From column #1 the stream passes through the column switching valve, and, depending upon the position of the valve, goes to either column #2 (the long molecular sieve column), or through variable restrictor #1. From the column switching valve the carrier gas passes to one side of the thermal conductivity cell.

The carrier gas stream that passes from the pressure gauge to the right hand rotameter goes through variable restrictor #2 to the column switching valve, and then goes to either column #2 (the longest molecular sieve column) or through variable restrictor #1, depending upon the position of the column switching valve. From the restrictor the carrier gas stream then passes through column #3 (the short molecular sieve column) to one side of the thermal conductivity cell (29:4).

In operation, a one milliliter sample is injected into the silica gel column with the column switching valve set with columns #1 and #2 in series. Neon, oxygen, nitrogen and carbon monoxide emerge from this column unseparated and pass into the first of the molecular

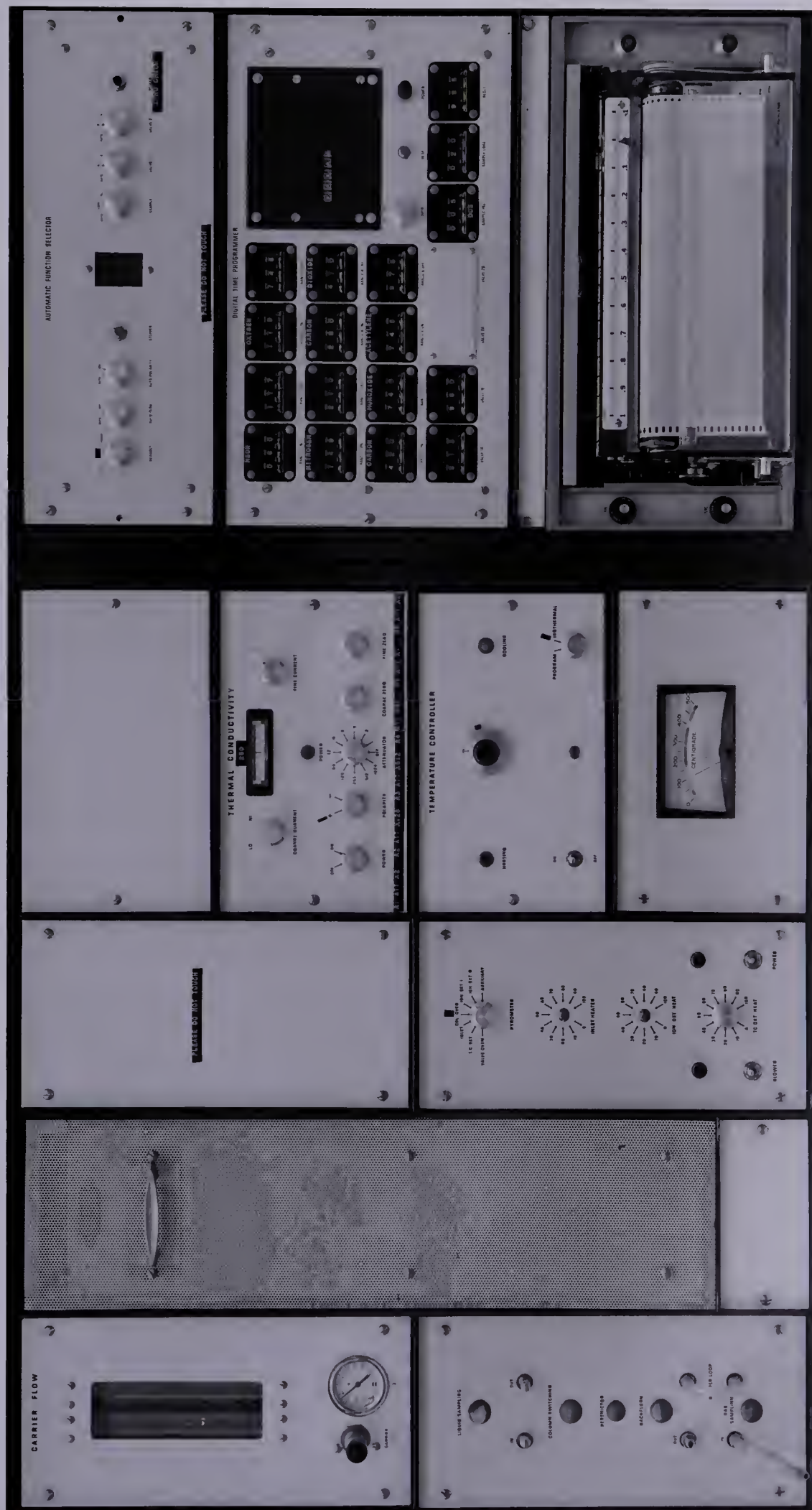


FIGURE 4: MICROTEK GAS CHROMATOGRAPH GC2013M

sieve columns (column #2). The silica gel column retains carbon dioxide and acetylene. The molecular sieve column separates neon, oxygen and nitrogen, as well as carbon monoxide, in that order, but as soon as the nitrogen has eluted, the column switching valve is actuated causing the carbon monoxide to pass into column #3. After the column switching valve has been actuated, the carbon dioxide elutes from the silica gel column followed by the carbon monoxide which has passed through column #3 to the detectors, on a different side of the Wheatstone Bridge from the other gases. Carbon monoxide is thus opposite to the others in polarity. After carbon monoxide is eluted, acetylene passes from the silica gel column to be detected.

Gas Separation

Gas separation using this system is by the physical means of elution analysis, as distinct from frontal and displacement analysis. In elution analysis, the carrier gas passes continually through the column and the mixture to be separated is introduced at the beginning of the first column. When the mixture enters the column it is mostly adsorbed, but an equilibrium between the column and the gas is set up in the interstices of the column so that some of the mixture always remains in the carrier gas. This portion moves along the column where it again equilibrates, and the material that was adsorbed previously begins to re-enter the gas phase to reach equilibrium with the clean carrier gas which follows up the zone of vapour. The process is shown in Figure 5, by arrows which show a model of a column with carrier gas shown flowing down the left hand side and the adsorbent as the stationary

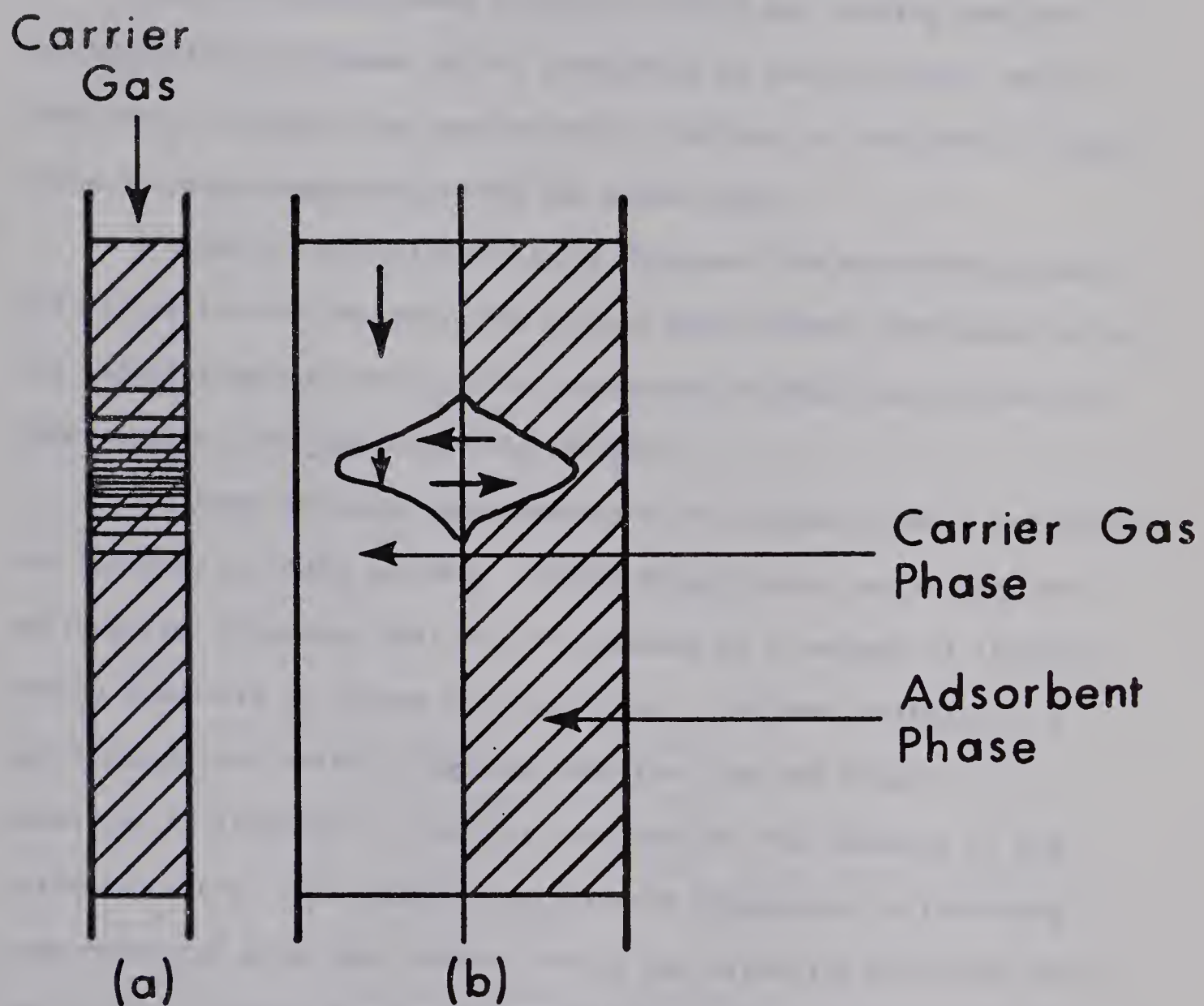


FIGURE 5 DIAGRAM OF A PERMEABLY PACKED COLUMN AND ITS IDEALIZATION IN WHICH GAS AND ADSORBED PHASES ARE REPRESENTED SEPARATELY. FROM LITTLEWOOD (25:2)

phase on the right hand side. "The interface between the phases is used as a length abscissa along the column, and positive ordinates in each phase represent the concentrations of the vapour therein" (25:2).

The process continues with the carrier gas leading the zone of vapour being stripped of its components by the adsorbent, while the vapour re-enters the carrier gas at the rear of the zone of vapour until it moves completely along the column (25).

A study of the effect of pore size upon the adsorptive qualities of silica gel has shown that, to a large extent, the selectivity of the material derives mostly from the molecular shape and size of the components of the sample mixture (34:371).

The term molecular sieve explains the manner by which separations are achieved by these columns. The molecular sieve has an open and well-defined structure that may be compared to a network of channels having diameters no larger than molecules. The mean pathway for a gas through this material depends upon the size and shape of its molecules in relation to the size and shape of the channels of the molecular sieve. The channels perform the separation by retarding some molecules more than others, and by not affecting molecules that do not fit. Carbon dioxide is completely adsorbed and is not released until the column is heated to high temperatures (12:829).

The Problem of Argon

When respiratory gases are analysed by conventional means, argon is included with the nitrogen concentration. However, in gas chromatographic analysis, the argon peak elutes at the same time as, and is

indistinguishable from, the oxygen peak. No practical techniques have yet been devised that will perform a separation of argon from oxygen, so a correction factor should be determined for use when knowledge of the absolute concentration of oxygen is required. Argon exists in the atmosphere at a concentration of approximately 0.94 per cent, but to merely subtract this constant from the oxygen concentration derived from chromatographic analysis is not a satisfactory solution.

An empirical correction must be applied to account for that part of the height of the oxygen peak that is due to the presence of argon. The method reported by Hamilton and Kory (12), may be used to make this correction. They used the following equation to determine the corrected height of the oxygen peak:

$$\text{Calc. } PH_{SO_2} = F_{SO_2} \times PH_{RO_2} / F_{RO_2}$$

where:

PH = peak height in millimeters,

SO₂ = unknown sample of oxygen,

F = fractional concentration (determined by Scholander analysis), and

RO₂ = reference sample of oxygen.

The difference between the observed oxygen peak height and the calculated oxygen peak height was assumed to be due to the presence of argon in the sample. Argon is chemically inert, and its concentration in the expired air is related to the nitrogen concentration in the same sample, and this relationship may be expressed by the equation:

$$\text{Obs. } PH_{UO_2} - \text{Calc. } PH_{UO_2} = (C) \times PH_{UN_2}$$

where:

PH_{UN_2} = peak height for the unknown sample of nitrogen at
the same attenuation as that used for oxygen,

(C) = the empirically determined constant, 0.015 in the
study quoted,

Obs. = observed.

The correction factor for argon could then be expressed by the
equation (12):

$$\text{Corr. } PH_{UO_2} = \text{Obs. } PH_{UO_2} - (C) \times PH_{UN_2}$$

and the corrected oxygen concentration in the respiratory gas samples
could be determined by:

$$F_{UO_2} = F_{RO_2} \times (\text{Corr. } PH_{UO_2} / PH_{RO_2})$$

It is essential that the reference gas used must not contain
argon, the nitrogen added to the mixture being pure and not derived
from room air. All other gas mixtures required for the following
techniques should be made up so that nitrogen is added to each mixture
in the form of air rather than pure nitrogen in order that the correc-
tion factors can be applied with consistency (24:145).

It has been reported though, that for samples collected from
subjects breathing gas mixtures, the need for a correction factor is
eliminated if the inspired gas mixture is used as the reference (12:836).

CHAPTER IV

METHODS FOR THE DETERMINATION OF RESPIRATORY EFFICIENCY AND CARDIAC FUNCTION

The two relevant methods of determining the respiratory efficiency and cardiac function are:

(a) the single-breath method for determining the diffusing capacity of the lung for carbon monoxide (9,10,31), and

(b) the single-breath method for determining the pulmonary capillary blood flow.

Before discussion of these techniques in turn, it is appropriate that the design of the apparatus used in the measurement of these parameters be discussed in full.

Apparatus for the Single-Breath Studies

Although a commercially produced, complete unit is available, the collection system for sampling the expired gases is not satisfactory for the determination of pulmonary capillary blood flow and the expense involved may be greatly reduced by making use of equipment already available in most laboratories, and having other equipment made to specification.

Respiration circuit. In order to provide a sufficient quantity of a special gas mixture to meet the requirement for an inspiration to forced residual capacity of the largest subjects, a Donald-Christie Bag-in-a-Box should be used, or failing this, a twelve liter glass

bottle approximately eighteen inches high and with a neck suitable for a large sized stopper (preferably four inches or more), may be specially made by glass blowers for a reasonable cost.

Two one and one-quarter inch holes must be drilled through the stopper and stainless steel T-unions made from one and one-quarter inch outside diameter tubing should be fitted through these holes. One of the T-unions should have a long vertical arm that should extend about two inches into the bottle from below the base of the stopper. To this projection is fitted a polyvinyl plastic meteorological balloon which will serve as the reservoir of the special inspiration gas mixture, or Inspiration Bag.

A length of one and one-quarter inch inside diameter polyvinyl thin wall plastic tubing is used to connect the T-piece fitted to the bag, to a one-way valve (to prevent a subject blowing back into the bag) and this valve is fitted to a Hans Rudolph four-way valve. The other end of this T-union is sealed with a stopper, but a small tube is passed through the centre and fitted externally with a small stopcock. This is to permit the inspiration system to be evacuated before each series of tests, and for dilling the bag with the inspiration mixtures.

One of the adjacent outlets from the Hans Rudolph valve is used to supply the subject with room air while he is getting ready for the test, while the other is used for exhalation after breath holding, and collection of the expired or "alveolar" sample.

Henceforth, all the ports, not including the mouthpiece, will be identified as follows:

(a) the port supplying normal air direct from the atmosphere will be known as Port #1,

(b) the port supplying the special gas mixture will be known as Port #2,

(c) the port leading to the expiration-collection system will be referred to as Port #3, and

(d) the remaining port, leading to atmospheric air, will be known as Port #4.

These ports should be selected in such a way that the subject may be switched directly from Port #1 to Port #2, and then to Port #3 and to Port #4 in sequence, with a clockwise (or anti-clockwise, if preferred) turn of the control tap.

From Port #3, exhaled gases pass directly through an eight inch by one and one-quarter inch outside diameter stainless steel tube which has been drilled and fitted with three nipples that fit straight on to stopcocks attached to the three fifty milliliter syringes that comprise the collection apparatus of the automatic syringe sampling system. The stainless steel tube is then connected by one and one-quarter inch inside diameter flexible plastic tubing to the other T-union fitted to the bag-in-the-bottle system. Another flexible plastic tube connects the other side of this T-union to a $13\frac{1}{2}$ liter wet spirometer. In this way, inspired volumes may be recorded on the spirometer recording paper because a volume drop in the inspiration bag due to inhalation is balanced by a drop in volume of the spirometer. Expired volume can be recorded directly.

The second spirometer outlet is fitted with a detachable stopper so that the expiration system can be flushed out after each trial.

All metal connections should be made from stainless steel because

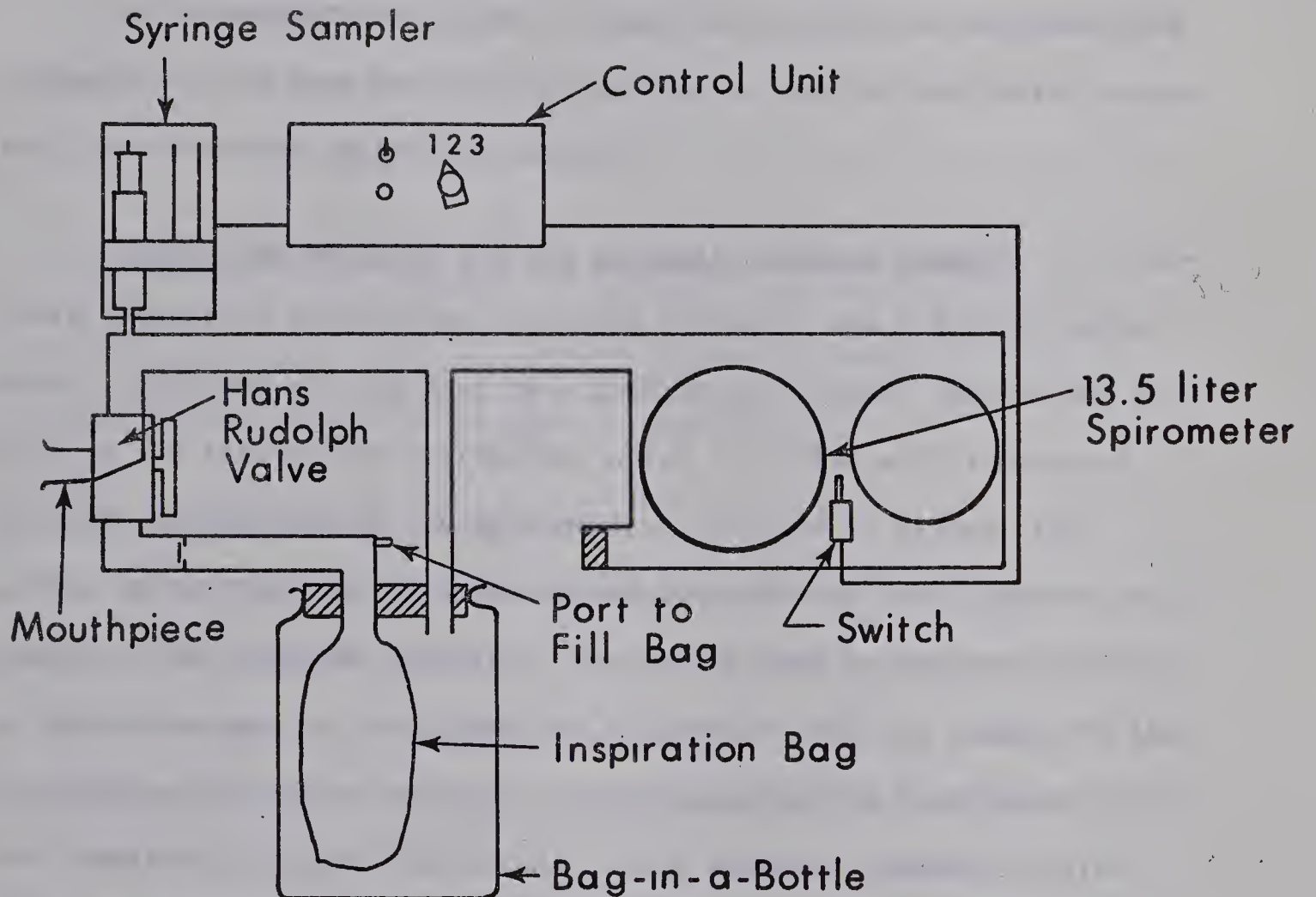


FIGURE 6 APPARATUS FOR USE WITH THE SINGLE BREATH TECHNIQUE

of the fact that acetylene reacts with brass and copper (16:120).

All tubing and bags should be polyvinyl plastic material as acetylene diffuses rapidly into rubber, and after a time, the rubber becomes hyper-saturated and releases acetylene back into the system.

If a Donald-Christie box is used, the inspiration bag should be connected in the same way as discussed above, and the box outlet should be fitted into the expiration circuit.

Electrical switches and the automatic syringe sampler. The complete cumulative inspiration recording system of the $13\frac{1}{2}$ liter spirometer is removed and replaced by a quarter inch square section rod as high as the tank of the spirometer, which is fitted with a base and attached to the body of the spirometer. This rod is fitted with a simple switch that can be moved up and down the rod and tightened to remain in any required position. The switch must be designed so that an upward movement of a striker arm attached to the pen support of the inspiration-expiration recorder (which occurs during inspiration) will not complete an electrical circuit, but a downward movement (during expiration of the subject) will cause the contacts to be forced together for sufficient time to complete a circuit.

The signal from the switch passes into a control unit which enables the operator to select the syringe that is to be used for collection of the sample. The electrical signal from the switch, interpreted by the control unit, then releases a catch that holds the appropriate syringe closed and empty. A spring automatically pulls back the stopper of the syringe and a fifty milliliter sample of the

expired gases is collected. Three syringes are fitted to the sampler unit at the University of Alberta, so that investigation may be made of the effects of sampling at different points during expiration of the special gas mixture. In this case, three switches are fitted along the rod on the spirometer and a circuit modification in the control box is required to allow the three syringes to sample in sequence.

For normal use, the control unit may be simplified to operate one syringe only during a trial, and the automatic sampler need be fitted with only one syringe. (The control unit circuit diagram for this type of use is shown in Appendix B and the design of a three-syringe automatic sampler is shown in Appendix A.)

Special Inspiration Gas Mixtures

For the measurement of diffusing capacity of the lung for carbon monoxide and pulmonary capillary blood flow, the same gas mixture is used. This mixture contains:

<u>Gases</u>	<u>Suggested Concentrations</u>
Neon (Ne)	0.25 - 0.50 per cent
Oxygen (O ₂)	20.00 per cent approximately
Nitrogen (N ₂) (from air)	79.00 per cent approximately
Carbon Monoxide (CO)	0.20 - 0.30 per cent
Acetylene (C ₂ H ₂)	0.20 - 0.40 per cent

A small reference gas cylinder to be used for calibration of the gas concentration of the other cylinders and for adjustment of the ranges of automatic gas chromatograph, should be purchased containing neon, oxygen, nitrogen, carbon monoxide, acetylene and carbon dioxide

(approximately six per cent).

The analysis of this mixture should be guaranteed and accurate to the second decimal. The nitrogen in this mixture must be pure to ensure that no argon is present.

Such certified mixtures are available from the Matheson Company of Whitby, Ontario and normal mixtures are available from Canadian Liquid Air of Montreal, Quebec.

Experimental Procedure

This procedure is common to both techniques, and the calculations may be made from the sample chromatogram analysis of the sample drawn after the breath-holding period.

The subject is allowed to rest quietly for several minutes after arriving in the laboratory, during which time the procedure is explained and demonstrated. The inspiration bag is then evacuated, filled with the inspiration mixture, flushed through the mouthpiece and re-filled. A sample is drawn from the circuit and analysed by the chromatograph.

The subject is then fitted with a nose clip and brought to the mouthpiece on the four-way valve (flushed with air to eliminate traces of the inspiration gas) and allowed to breathe through Port #3 into the expiration circuit. The subject is instructed to inhale maximally, and then to exhale maximally so that the total lung capacity can be recorded. This procedure is repeated several times (the carbon dioxide absorber is removed so the spirometer must be flushed out each time) so that an average total lung capacity can be calculated. The subject is then asked to repeat the same procedure, but to inhale as much as possible

without straining. This inspiration should be about 200-300 milliliters short of the total lung capacity. The reproducibility of this inspiration is stressed, and the subject is allowed several repetitions to enable him to get used to inspiring to the same level each time.

The subject is then allowed to rest, and the electrical switch is positioned on its shaft so that, if the subject continues to make inspirations to a reproducible inspired volume, the striker arm will activate the switch on expiration, after 800 milliliters (equivalent to the dead space) has been exhaled. It may be of assistance to mark the required inspiration level on the spirometer chart so the subject may see it.

The subject is then readied for the series of trials, and fitted with electrocardiograph leads, a nose clip and mouthpiece. The tap on the Hans-Rudolph valve is turned so that the subject breathes room air through Port #1. The electrocardiograph may be run for the duration of the trial at a slow speed and a stimulus button used to mark the record during the breath-holding period.

On request, the subject completely exhales through Port #1 and signals by snapping his fingers when he can exhale no more air. At this signal the control tap is turned to Port #2 and the subject told to inhale as rapidly as possible to the required volume and to then hold his breath. When breath-holding commences, the control tap is turned to a neutral position between Ports #2 and #3 so that no air exchange can occur.

At the end of the desired breath-holding period, which may be between three and four seconds or between seven and ten seconds, the tap

is turned to Port #3 and the subject is instructed to exhale rapidly. After the sample has been collected, the control tap is turned to Port #4 and the subject is allowed to remove the mouthpiece.

The collection syringe should be removed from the apparatus immediately and flushed through the chromatograph. After a one or two second delay to allow pressures to equalise, the chromatograph sample injector is activated and the sample taken up for analysis.

A five to ten minute rest period should be allowed between trials, and the length of this period may coincide with the analysis time of the chromatograph, so that collected samples need not be left in storage. This rest period is to allow the special gases to be removed completely from the lungs, and a two to four minute period is sufficient. There should be at least four repetitions at rest so that sufficient points can be calculated of the disappearance curves of the two gases. Two of these trials should be at short breath-holding times, and two at longer breath-holding times. For exercise trials, a maximal breath-holding time of five seconds is recommended, both for the convenience of the subject and, more important, to ensure that there is no re-circulation of acetylene.

Diffusing Capacity of the Lung for Carbon Monoxide

The transfer of gases across the pulmonary membrane from the alveoli to the capillaries, and vice versa, is performed by a process of diffusion. If diffusion is expressed in terms of pressure, then gases will move from an area of high gas pressure to an area of low gas pressure until equilibrium is attained. The speed with which the

equilibrium is reached is related to the pressure difference across a membrane that exists between the two areas of differential pressure. In the lung, this pressure difference is termed the alveolo-capillary pressure gradient. Most gases reach an equilibrium within the lung very rapidly and the amounts of these gases that can be transferred are limited only by ventilation and blood flow. Due to the fact that oxygen and carbon monoxide combine chemically with the haemoglobin, much greater quantities of these gases must be transferred before equilibrium can be reached. Under certain conditions, as when the efficiency of the membrane is impaired, oxygen and carbon monoxide cannot reach equilibrium during the time that the blood remains in the capillaries (13:18).

Tests of pulmonary diffusing capacity are made in order to evaluate the efficiency of the transfer of gases from the lung to the capillaries.

The measure of pulmonary diffusing capacity relates the transfer of gas to the difference in the mean pressure of that gas between the alveoli and the capillaries. This may be expressed by the equation (13:17):

$$\text{Diffusing Capacity (DL)} = \frac{\text{Quantity of Gas Transferred}}{\text{Mean alveolar pressure of the gas} - \text{Mean pulmonary capillary pressure of the gas}}$$

Diffusing capacity of the lung is affected by two factors, the effective surface area of the lung and the thickness of the pulmonary membrane. The rate of transfer of gas into the pulmonary capillaries is proportional to the area available for gas transfer, and if the area is reduced by damage or removal of some of the alveoli, gas transfer is

reduced per unit time (13). Similarly, if the surface area is increased through greater expansion of the lung, gas transfer may be increased (30:498).

The rate of gas transfer is inversely proportional to the distance that the gas must diffuse and consequently, if the membrane is thickened, there will be a reduction in the amount of gas transferred across the membrane per unit time (13:18).

The measurement of the diffusing capacity of the lung for oxygen is difficult as separate analyses are required of the oxygen tension of the alveoli, the pulmonary vein and the pulmonary artery, and a mathematical derivation of the mean gas tension in the alveolar capillaries must be calculated. Although the technique has been used, it is difficult and time-consuming. It is usual to measure the diffusing capacity of the lung in terms of the transfer of carbon monoxide across the membrane.

Carbon monoxide combines readily with haemoglobin, and is present in the blood in extremely small concentrations. As carbon monoxide bonds readily with haemoglobin, the capillary gas tension will remain at approximately zero provided that the subject refrains from smoking for several hours before the test. Therefore, only the rate of carbon monoxide transfer and the alveolar carbon monoxide tension need be measured in order to calculate the diffusing capacity (13:19).

If the alveolar tension of carbon monoxide is known for two points of time, then the rate of the disappearance of carbon monoxide into the alveolar capillaries may be determined. The slope of the disappearance rate may be assumed to follow a linear exponential disappearance curve

and this slope may be used in the calculation of the rate of gas transfer for determining the diffusing capacity of the lung for carbon monoxide.

The single breath technique is based upon the assumption by Krogh (22), that the rate of disappearance of carbon monoxide from the alveolar gas during a breath-holding period is proportional to the concentration present. The Krogh technique involved breathing a mixture of carbon monoxide in room air, and immediately expelling about a liter of that air and holding the remainder in the lungs for a period of time. The sample taken immediately after inspiration was assumed to be equivalent to the concentration within the lungs before gas transfer could occur. The breath-holding time was timed from the end of the collection of the first sample to the end of collection of the second sample.

The Krogh method was modified by Forster and his co-workers (9, 10) and standardised for clinical measurement by Ogilvie, et al. (31). Helium or some other suitable inert gas was found to be suitable for use in determining the dilution of the inspired gas mixture in the residual air of the lung so that the initial concentration of the gases at the alveoli could be calculated.

Gas chromatography has been applied to the analysis of the exhaled gases, and as helium is commonly used as a carrier gas with this type of analysis, neon was substituted for helium for the measurement of dilution.

Calculations. In all calculations involving fractional concentrations of the gases, it is convenient to use the chromatographic peak

height response directly, instead of making additional calculations. If this is to be done though, the alveolar samples must be compared to samples of the gases taken from the inspiration bag prior to breath-holding. This procedure is followed throughout the computer programme developed to assist in reducing the time required for treatment of the data.

Several preliminary calculations must be made before the main diffusing capacity equation is computed. These relate to the determination of the inspired volume, breath-holding time and alveolar volume. The measurement of the inspired volume, breath-holding time, peak height responses of the inspiration bag sample and those of the alveolar sample, are all the manual calculations that are required if the computer programme is used.

1. Inspired volume. This may be measured directly from the spirometer recording for each trial and corrected for standard temperature and pressure (dry).

2. Alveolar volume (STPD). The alveolar volume is the actual volume of the lung from which diffusion takes place. It is calculated by the following equation:

$$V_A(\text{STPD}) = V_I(\text{STPD}) \times F_{I\text{Ne}} / F_{A\text{Ne}}$$

where:

$V_A(\text{STPD})$ = alveolar volume STPD, in milliliters,

$V_I(\text{STPD})$ = inspired volume STPD, in milliliters,

$F_{I\text{Ne}}$ = fractional concentration of neon in the inspired gas mixture,

$F_{A\text{Ne}}$ = fractional concentration of neon in the alveolar sample.

3. Breath-holding time. If the spirometer kymograph drum is switched to its fast speed during the test period, the breath-holding time may be read directly from the chart on the drum, as it is calibrated vertically at one second intervals (one second equals 32 millimeters of chart travel).

In an analysis of the reported anomalies of the technique, Jones and Meade (17) found that the anomalies were eliminated when using different breath-holding times, if the time was calculated using a correction for a positive intercept in the disappearance slope of carbon monoxide. The time required for the slope to reach unity was found to be equivalent to three-tenths of the inspiration time. Therefore, the breath-holding time is equal to the time from the beginning of inspiration, to the mid-point, in time, of the sampling period, less three-tenths of the inspiration time.

4. Diffusing capacity of the lung for carbon monoxide. The equation used for the calculation of this parameter was given by Krogh (22), and is still applicable.

$$D_{LCO} = \frac{V_A \times 60}{(P_B - 47)} \times \frac{1}{\Delta t} \times \log_n \left[\frac{F_{ACO.o}}{F_{ACO.t}} \right]$$

where:

D_{LCO} = diffusing capacity of the lung for carbon monoxide in milliliters carbon monoxide STPD/minute/millimeters of mercury carbon monoxide tension,

V_A = alveolar volume STPD in milliliters,

$(P_B - 47)$ = barometric pressure less the pressure of water vapour in the alveolar volume,

Δt = breath-holding time in seconds,

$\log_n$ = natural logarithm,

$F_{A_{CO.o}}$ = the initial concentration of carbon monoxide in the lung before diffusion occurs. This is derived from the equation: $F_{A_{CO.o}} = F_{I_{CO}} \times F_{A_{Ne}} / F_{I_{Ne}}$ (where $F_{I_{CO}}$ is the concentration of carbon monoxide in the inspired mixture, $F_{A_{Ne}}$ is the concentration of neon in the alveolar sample, and $F_{I_{Ne}}$ is the concentration of neon in the inspired neon).

$F_{A_{CO.t}}$ = the fractional concentration of carbon monoxide in the alveolar sample.

This equation may be used for the individual calculation of each trial at rest, and must be used for the exercise calculations. It is possible to use an equation using the average alveolar volume of the resting trials, in an equation using the slope of the disappearance of carbon monoxide. The slope of carbon monoxide is determined by drawing a graph with breath-holding time on the X axis and the logarithm of the equation ($F_{A_{CO.t}} / F_{A_{CO.o}}$) on the Y axis. It is convenient to use semi-logarithm paper for this purpose. A regression line is drawn through the points (derived from four resting trials at various breath-holding times) and the logarithm of the slope calculated for a ten-second period is used in the following equation (18):

$$D_{L_{CO}} = \frac{13816}{(P_B - 47)} \times V_A \text{ in liters} \times \log \left[\frac{\frac{F_{A_{CO.t}} \text{ after 2 seconds}}{F_{A_{CO.o}}}}{\frac{F_{A_{CO.t}} \text{ after 12 seconds}}{F_{A_{CO.o}}}} \right]$$

Both equations are included in the computer programme, with all trials worked out individually in Columns #1 to #7 of the matrix array and by the slope method in column #8 of the answer matrix; a similar presentation is made in the titled answer sheet with the answer calculated

by the slope method given opposite the title, and the seven individual answers given below.

Discussion. The early studies by Forster, et al. (9,10) and Ogilvie, et al. (31) indicated that the estimate of diffusing capacity of the lung for carbon monoxide varied with breath-holding time, inspiration time and the manner in which the sample was collected. Uneven distribution of the inspired mixture was thought to be the reason for these anomalies, but Jones and Meade (17) showed that, if the breath-holding time was modified by making a correction for changes in the alveolar concentration of carbon monoxide during inspiration and expiration, and if small samples were taken, these anomalies would be corrected. The authors did not imply that the lung gases were evenly distributed, but felt that the normal complexity of distribution was not observable by the technique.

Apart from the problem with diffusing capacity decreasing with increases in breath-holding time, which was explained above, Ogilvie, et al. (31) reported the following factors that influenced diffusing capacity measurements;

1. The portion of the exhalate sampled. This was believed to be likely to affect the measurement of diffusing capacity of the lung for carbon monoxide, but if the first 750 milliliters of exhaled air is allowed to pass through the collection system before sampling, it was found that it did not matter which part of the exhalate was collected and used to make the computations as there was only an average discrepancy of 10 per cent. Therefore,

. . . Even if the inspired gas is distributed unevenly to the different alveoli, if it is distributed without regard to the diffusing capacity of each alveolus, any sample of expired alveolar gas will give the same value of D_L as any other, albeit not the correct total D_L . (31:5)

2. Intra-thoracic pressure. There is a development of pressure in the lungs during breath-holding, whether the chest is relaxed or not, The measurement of diffusing capacity during the performance of a Valsalva Manoeuvre decreases the value of diffusing capacity by up to 17 per cent and the increases in pressure would be expected to have some effect upon the cardiac output because of the constriction of the great veins. For this reason, it is best that the volume of the gas taken into the lung for breath-holding be limited to about 200 milliliters below the total lung volume (about functional residual capacity) (30:493).

3. Variation in lung volume. These did not appear to have an excessive effect upon the measurements of diffusing capacity, although a study by Miller and Johnson (30) did indicate that there was a significant increase in diffusing capacity due to an increase in membrane diffusion of the lung with inflation from functional residual capacity to total lung capacity.

4. Body position. The postural position of the subject during the test had an effect upon diffusing capacity, with measurements taken with the subject supine being significantly greater than those recorded with the subject in other positions.

5. Variations in alveolar oxygen tensions. Diffusing capacity of the lung for carbon monoxide decreases as the oxygen tension in the alveoli is raised. If a subject breathes pure oxygen, the diffusing

capacity value may be halved.

6. The importance of venous carbon monoxide back-pressure. If a subject has a significant amount of carbon monoxide already bonded to the haemoglobin in the red blood cells due to heavy smoking, further diffusion of carbon monoxide across the membrane will be impeded because of the plasma carbon monoxide tension that will exist in equilibrium with that bonded to the haemoglobin. For this reason, back-pressure of carbon monoxide should be calculated if smokers are tested and a correction made to allow for this back-pressure in the computations.

This correction was not included in the equations that formed the basis for the computer programme included in this study as the subjects drawn from the university population can usually be relied upon to refrain from smoking for several hours before a test. In extreme cases an eight per cent error could be generated by the operation of this factor.

7. Repetition of the test. The inspired gases can be expected to be removed from the lung after approximately two minutes of resting breathing. There will be an increase in the back-pressure of carbon monoxide after each breath-holding test, but this increase was found to be insignificant even when several repetitions of the test were made in quick succession.

8. The effects of exercise. A moderate to heavy exercise can produce 46 per cent increases in the diffusing capacity of the lung for carbon monoxide. These changes may be expected to return to normal within two to three minutes of the cessation of the exercise. For standardisation of the test procedure, it is best to allow the subject to rest quietly for several minutes before performing resting

determinations, so that the effects of any exercise involved in coming to the laboratory may be eliminated.

9. The effects of body surface area. Diffusing capacity was found to be correlated to weight, height and body surface area, and there was a general increase with increasing body size. Thus, body surface area should be taken into account when predicting a subject's normal diffusing capacity.

These factors all point to the necessity of developing a standardised testing procedure. In particular, the position of the subject when tested, his smoking prior to the test, his recovery from any exercise involved in attending the laboratory, his activity while at the laboratory and the conduct of the experiment itself should be rigorously controlled.

Ogilvie, et al. (31:11) presents data to indicate that the average normal diffusing capacity of the lung for carbon monoxide is 24.9 milliliters per minute per millimeter of mercury. A prediction formula was developed using the equation:

$$D_{L_{CO}} = \text{Body surface area (in square meters)} \times 18.85 - 6.8.$$

Pulmonary Capillary Blood Flow

The single-breath technique was applied to the investigation of pulmonary capillary blood flow when Cander and Forster (4) used various inert, soluble gases, such as acetylene and nitrous oxide for the measurement of pulmonary capillary blood flow and the pulmonary tissue volume, and inert, insoluble gases for the estimation of the dilution of the inspired gases in the residual volume of the lung.

They felt that in view of the many criticisms and reported inaccuracies of the foreign gas methods, it was best to develop a new method as they believed that they could circumvent two of the major weaknesses of the other tests, namely, the difficulty involved in obtaining a uniform sample of the concentration of the inspired mixture before diffusion into the blood cells, and the possibility of re-circulation of the dissolved gases back to the lungs during the testing period.

In using the single-breath technique, and including helium in the inspired mixture, they were able to measure the dilution of the relatively insoluble helium in the lung, and infer that this dilution would be the same as occurred to the soluble gases as they entered the lung.

It was discovered that there was not only a decrease in the concentration of the soluble gas due to its dilution in the residual volume and its diffusion into the blood, but there was also a rapid initial fall in the concentration of the acetylene and nitrous oxide at a greater rate than was the case with the later diffusion. This they found to be due to the diffusion of the gases into the pulmonary parenchymal tissue volume. This diffusion was then used to calculate the parenchymal tissue volume of the lung so that a correction factor could be applied in the calculation of pulmonary capillary blood flow.

The rapid initial solution of the soluble gas into the tissue volume of the lung was evidenced by the dropped intercept of the acetylene and nitrous oxide disappearance curves.

The technique was further refined by Johnson, et al. (19) by

the application of gas chromatography to the analysis of gases, and by combination of the procedure with that of Ogilvie, et al. (31), so that diffusing capacity of the lung for carbon monoxide and pulmonary capillary blood flow and tissue volume could be determined simultaneously.

Calculation. The determination of pulmonary capillary blood flow is based upon the known capacity of acetylene to dissolve into the red blood cells at a constant rate.

The Bunsen solubility of acetylene in the red blood cells was determined by Grollman (11) to be .740 milliliters of gas/milliliter of blood/atmosphere at 37°C. Chapman, et al. (5), however, stated that the solubility coefficient had been determined in their laboratory to be .7002. Grollman's figure is used because of its acceptance by Johnson, et al. (19), on the understanding that the results may be six per cent below the expected values for this reason.

The Bunsen solubility of acetylene into the pulmonary parenchymal tissue was found by Cander (3), to be .768 milliliters of gas/milliliter of tissue/atmosphere at 37°C.

In all equations referring to fractional concentrations of the various gases, the peak height response in millimeters may be substituted, provided that the chromatograph response of the gases in the inspiration mixture before breath-holding is used as the reference to which the alveolar analysis is compared.

In order to calculate the pulmonary parenchymal tissue volume and the pulmonary capillary blood flow, the disappearance curve of acetylene must first be established, and it is essential that there should be at

least four repetitions of the test at rest, using two long (approximately eight seconds) and two short (approximately four seconds) breath-holding periods so that an accurate regression line may be drawn.

The disappearance ratio is plotted for each breath-holding time on the X axis and the logarithm of the ratio:

$$\frac{F_{AC_2H_2.t}}{F_{AC_2H_2.o}} \text{ on the Y axis}$$

where:

$F_{AC_2H_2.t}$ is the alveolar concentration of acetylene after the breath-holding,

$F_{AC_2H_2.o}$ is the initial concentration of the acetylene in the alveoli before dilution takes place,

therefore,

$F_{AC_2H_2.o}$ = the concentration of acetylene in the inspiration bag multiplied by the ratio of the alveolar neon concentration to the inspired neon concentration.

1. Pulmonary parenchymal tissue volume. Cander and Forster (4) developed the equation for tissue volume, which follows:

$$V_t = \frac{V_A}{\alpha_t} \left[\frac{100}{\text{Intercept at } t_0 \text{ in } \%} \right] \left(\frac{760}{P_B - 47} \right)$$

where:

V_t = pulmonary parenchymal tissue volume in milliliters,

V_A = alveolar volume in milliliters,

Intercept at t_0 in percent

= the intercept of the regression line drawn on a semi-logarithmic graph, with the logarithm of the alveolar concentration of acetylene divided by the initial concentration of acetylene before dilution, on the Y axis and the breath-holding time on the X axis; expressed as a percentage

$(P_B - 47)$ = barometric pressure corrected for the pressure of water vapour in the alveolar volume, in millimeters of mercury,

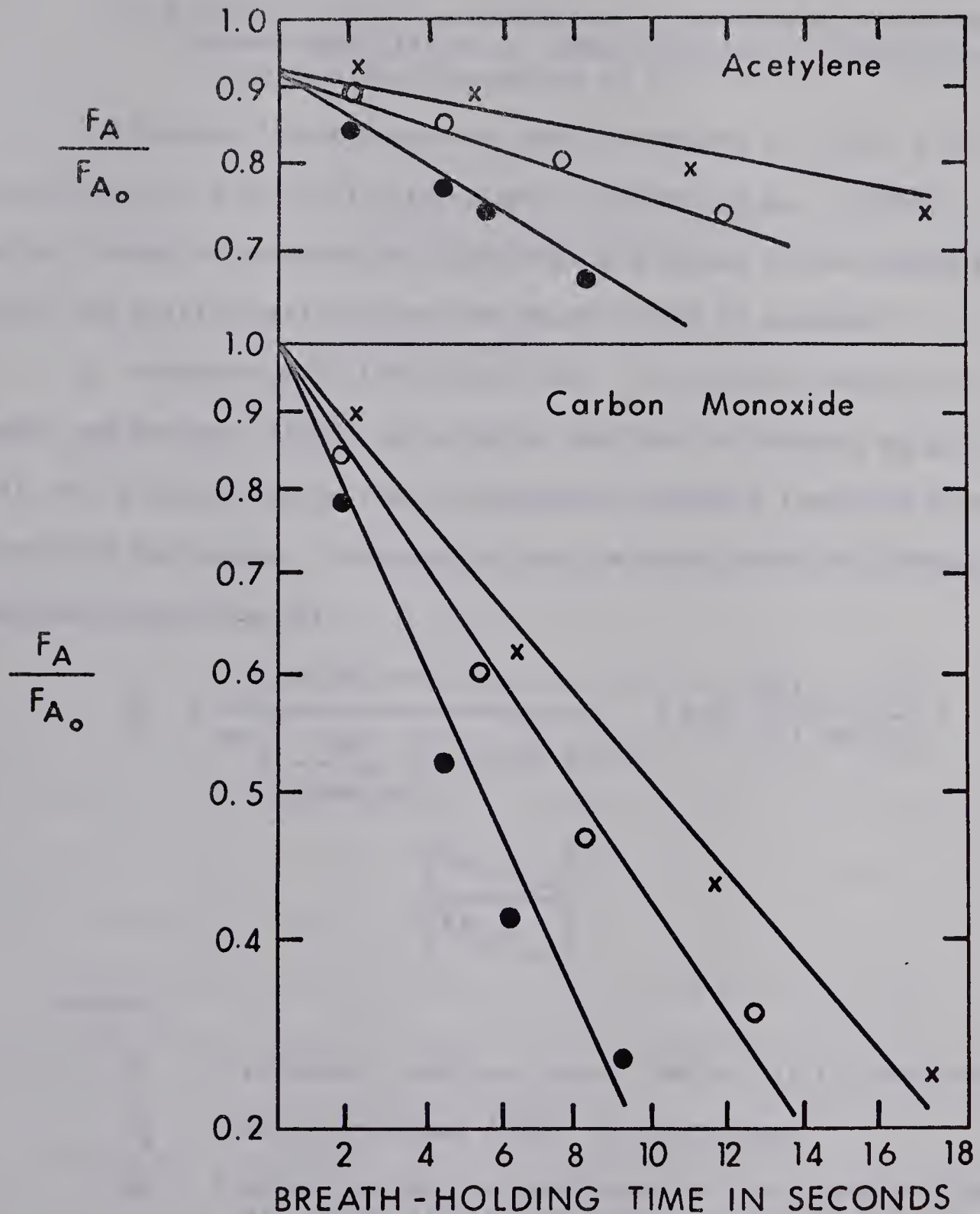


FIGURE 7 SIMULTANEOUS DISAPPEARANCES OF ALVEOLAR ACETYLENE AND CARBON MONOXIDE DURING BREATH HOLDING. MEASUREMENTS WERE MADE DURING A VALSALVA MANEUVER (x), DURING REST (o) AND AT 5 MPH ON A 4 DEGREE GRADE (●). FROM JOHNSON, ET AL. (19:894)

α_t = bunsen solubility coefficient of acetylene in pulmonary parenchymal tissue, at .768 milliliters of gas/milliliter of tissue/atmosphere at 37°C.

The average tissue volume has been determined by Cander and Forster (4) to be 627 milliliters, while Johnson, et al. (19:896) tested a group of subjects and found that the tissue volume ranged from 410 to 760 milliliters; figures that appear to be in agreement.

2. Pulmonary capillary blood flow. The original equation of Cander and Forster (4:548) was slightly modified by Johnson, et al. (19:894), but a further correction is required to convert the blood flow to blood flow per minute. The equation for the calculation of pulmonary capillary blood flow is:

$$\dot{Q}_c = \frac{V_A \times 760 \times 60}{\alpha_B \left[\frac{V_A}{V_A + \alpha_t \cdot V_t} \right] (P_B - 47) \times \Delta t} \times \log_n \left[\frac{V_A}{V_A + \alpha_t \cdot V_t} \right] \times \left[\frac{F_{AC_2H_{2.o}}}{F_{AC_2H_{2.t}}} \right]$$

where:

$\dot{Q}_c$ = pulmonary capillary blood flow in milliliters/minute,

V_A = alveolar volume (STPD) in milliliters,

α_B = Bunsen solubility coefficient of acetylene in blood, at .740 milliliters of gas/milliliter of blood/atmosphere at 37°C.

α_t = Bunsen solubility coefficient of acetylene in pulmonary parenchymal tissue, at .768 milliliters of gas/milliliter of tissue/atmosphere at 37°C.

V_t = tissue volume of the lung in milliliters,

Δt = breath holding time as determined by Jones and Meade (17:139).

$(P_B - 47)$ = barometric pressure less the pressure of water vapour in the alveolar volume, in millimeters of mercury,

$\log_n$ = natural logarithm,

$F_{AC_2H_2.0}$ = fractional concentration of acetylene in the lung before any dilution of diffusion has occurred,

$F_{AC_2H_2.t}$ = fractional concentration of acetylene in the alveolar sample.

Discussion. Apart from the inaccuracies mentioned previously, that had been the cause of much of the underprediction associated with the foreign gas methods in comparison with the Direct Fick Techniques, various other small problems remain.

Any right to left shunt across the pulmonary capillary bed that allows blood to pass through the pulmonary circulation without being oxygenated in the alveoli will not be accounted for by this technique. Thus, there could be a 2.2 per cent underprediction of cardiac output using this method (4:550).

Any recirculation of acetylene into the lungs after a long breath-holding period may be recognised as a change in the slope of the disappearance curve and avoided (19:899).

The alveolar volume is over-estimated by an amount equivalent to the volume of the anatomical dead space and this could make estimates of the pulmonary capillary blood flow about three per cent too large (19).

The absolute values of residual volume as calculated by the single breath method are higher than those determined by nitrogen wash-out, but there is no additional increase during exercise (19).

Non-uniformity of blood distribution to the alveolar capillaries

of the lung may cause errors in estimates of blood flow in much the same way that uneven distribution affects the diffusing capacity measurements (19).

The improvements over the Grollman Technique (11) may be listed as:

1. recognition of the appearance of acetylene recirculation by a change in the disappearance curve,
2. incorporation of a correction for acetylene solution into the pulmonary parenchymal tissue in the initial period of inspiration,
3. an accurate calculation of the initial concentration of the acetylene at the alveoli before the diffusion of the gas into the blood, or solution into the tissue occurs.

It is reasonable then to expect results that are comparable to values of cardiac output and stroke volume determined by the Direct Fick Methods. Brandfonbrener (2) reported that for male subjects of a mean age of 23.6 years, the cardiac output was 6.49 ± 0.51 liters/minute and the cardiac index was 3.72 ± 0.28 liters/minute/square meter of body surface area, when determined by the Direct Methods. He also quoted stroke volume to be 85.6 ± 6.1 milliliters/beat and a mean stroke index of 48.9 ± 3.1 milliliters/beat/square meter of body surface area for the same subjects.

Published reports by Cander and Forster (4) and Johnson, et al. (19) show that the technique is capable of close prediction of cardiac output from pulmonary capillary blood flow data.

CHAPTER V

COMPUTER PROGRAMMING OF SELECTED METHODS INVOLVED IN CARDIO-PULMONARY RESEARCH

The measurement of pulmonary diffusing capacity of the lung for carbon monoxide and pulmonary capillary blood flow may be made following one series of tests and the amount of calculation required is considerable. To reduce the amount of time that must be spent in computation, the computer programme TRIAL was developed. This programme has been written so as to be applicable to a wide range of testing situations, and, with minor alterations, to different computers.

The programme is made up of several different types of cards or decks of cards. These are:

1. monitor control cards,
2. mainline programme deck,
3. sub-routine programme deck,
4. subject control cards,
5. data cards, and
6. final card.

Details for the preparation of all these cards are given in Appendix D.

Monitor Control Cards

These may vary depending upon the type of computer system employed. The University of Alberta uses the IBM7040 Operating System (IBSYS), which makes available an integrated set of programmes to take

care of the details of putting job programmes into the computer, getting the results out, and handling problems involved in interrupting faulty programmes. The appropriate cards for this programme, using the IBSYS system are:

1. \$IBSYS card,
2. \$JOB card,
3. \$TIME card,
4. \$IBJOB card,
5. \$IBFTC card, and
6. \$ENTRY card.

These monitor control cards have such functions as identification of the job, providing time and output limits, calling in the processing monitor to perform the requested routine options, and to indicate the end of the storage load (23:21).

Mainline Programme

The programme is written in Fortran IV (1,27), which is almost universally applicable, and is used on the assumption that the programme may be used without change on most computer systems presently available.

Some features of the Fortran IV are not available in all implementations, and it is advisable to discuss the programme with a systems engineer to see if it can be applied unchanged to the local computer.

The programme includes many "comment" cards, these being identified by the letter "c" in the first column of the card. The main operations are explained throughout the programme and the significant computations are identified. The location of each answer in the matrix

of results is also shown. A complete list of all the computation processes, also showing the answer locations, is given at the end of the mainline programme. Using these comment cards it is possible to follow all the calculations as they are made, and to identify the elements of each equation as it is computed.

A feature of the programme is the fact that it offers a choice in the manner of presentation of the answers. Normally, the output that would be desired would be the one listing, and titling, the most significant answers, as well as showing the subject's name and the date of the test. If, however, the researchers wishes to have a full listing of all the answers generated by the programme, these may be listed in the form of a matrix of the sixty answers for up to seven trials, with the eighth column of answers showing information derived from mean values or pooled data to give the average results or the results of regression analyses.

The programme is capable of handling any combination of resting and exercise trials up to a total of seven, but as at least four resting determinations are required for the accurate computation of the disappearance curves of carbon monoxide and acetylene, the exercise trials are effectively limited to three. This, however, is sufficient for many standardised exercise tests.

Some of the cards in the programme require special mention, and as each card is numbered cumulatively in columns #78-80, they are easy to identify for discussion. Card TRIAL #96, which reads "MZ = 5" must be altered if the computer to be used, uses a different numeral to

identify the READ a card operation. The University of Alberta uses the numeral "5" to identify this operation, and the numeral "6" to identify the WRITE operation. In order to read card TRIAL #78 (the format card for the subject control card) the computer must know the different codes in advance.

The subtraction "-85" from the calculated alveolar volume on card TRAIL #124 refers to the deduction that should be made to account for the dead space of the apparatus. This volume (in milliliters) will change with each design.

The regression equations to determine the disappearance rates of acetylene and carbon monoxide over time, are performed by cards numbered TRIAL #196-209 and from TRIAL #220-227. The formulae used to perform these operations are standard regression equations for the determination of the slope (β) and the intercept (α) of the disappearance curves of the gases (8:120):

$$\beta_{yx} = \frac{N\sum XY - (\sum X \cdot \sum Y)}{(\sum X^2 - (\sum X)^2)}$$

$$\alpha_{yx} = \frac{\sum Y}{N} - \beta \frac{\sum X}{N}$$

where:

β_{yx} = the slope of the regression line of the Y values on the X values, where the Y values refer to the ratios of the alveolar to the initial concentrations of the gases,

N = the number of cases,

$\sum XY$ = the sum of the products of X and Y,

$\sum X$ = the sum of the values of X,

$\sum Y$ = the sum of the values of Y,

$\sum X^2$ = the sum of the squared values of X,

$\sum Y^2$ = the sum of the squared values of Y, and

$\angle_{xy}$ = the intercept of the regression analysis of the Y values on X.

Prediction formulae are included in the programme for total lung capacity, pulmonary parenchymal tissue volume, diffusing capacity of the lung for carbon monoxide and cardiac output. The formulae were developed by Johnson (18) for comparison between obtained and expected values of pulmonary function.

Sub-Routine Programme Deck

The sub-routine TRIAM is used only for the presentation of the answers in a written format. The name of the subject, the date of the test, and the significant answers are all titled and listed, with the mean values and pooled data results listed on the far right on the same line as the title, and the separate answers of each trial given on the line below the title, in order from the left.

This sub-routine may be by-passed by requesting the sixty answer matrix presentation of answers, by indicating the desired preference on the Subject Control Card.

Subject Control Card

This card is placed immediately in front of the data and contains the information concerning the input and output device codes that perform the READ a card and WRITE operations, the number of resting and exercise tests, the output selection, the full name of the subject and the date of the test as well as an identification number.

Data Cards

Two cards should be prepared for each trial performed by a subject. The appropriate columns reserved for each measurement are shown on comment cards in the body of the mainline programme, and the format should be adhered to. No decimal points need be punched onto the cards. With regard to the measures of oxygen peaks, for accuracy over a wide range of concentrations, it has been found that a measurement of the integrated area is more accurate than peak height. If the recorder used is not fitted with an integrator, peak area should be used in all oxygen measurements.

Time #1 is incorporated as a measure that could be used for investigation of diffusion up to two time points during expiration of the special gas mixtures.

Final Card

A single blank card should be added to the back of the deck, after the last data card. This is to signify the end of the input data.

Order of Cards and Decks

The order of cards when using the IBSYS system is:

1. \$IBSYS, \$JOB, \$TIME, \$IBJOB, and \$IBFTC monitor system cards,
2. Mainline programme TRIAL deck,
3. \$IBFTC card for sub-routine TRIAM,
4. Sub-routine programme TRIAM deck,
5. Subject Control Card,
6. Data cards of first subject,

7. Control card of second subject, if any,
8. Data cards of second subject, if any,
9. Control Cards and Data Cards of subjects 3 to n, and
10. Blank card.

There must be a control card and data cards for every subject whose data is to be processed.

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REFERENCES

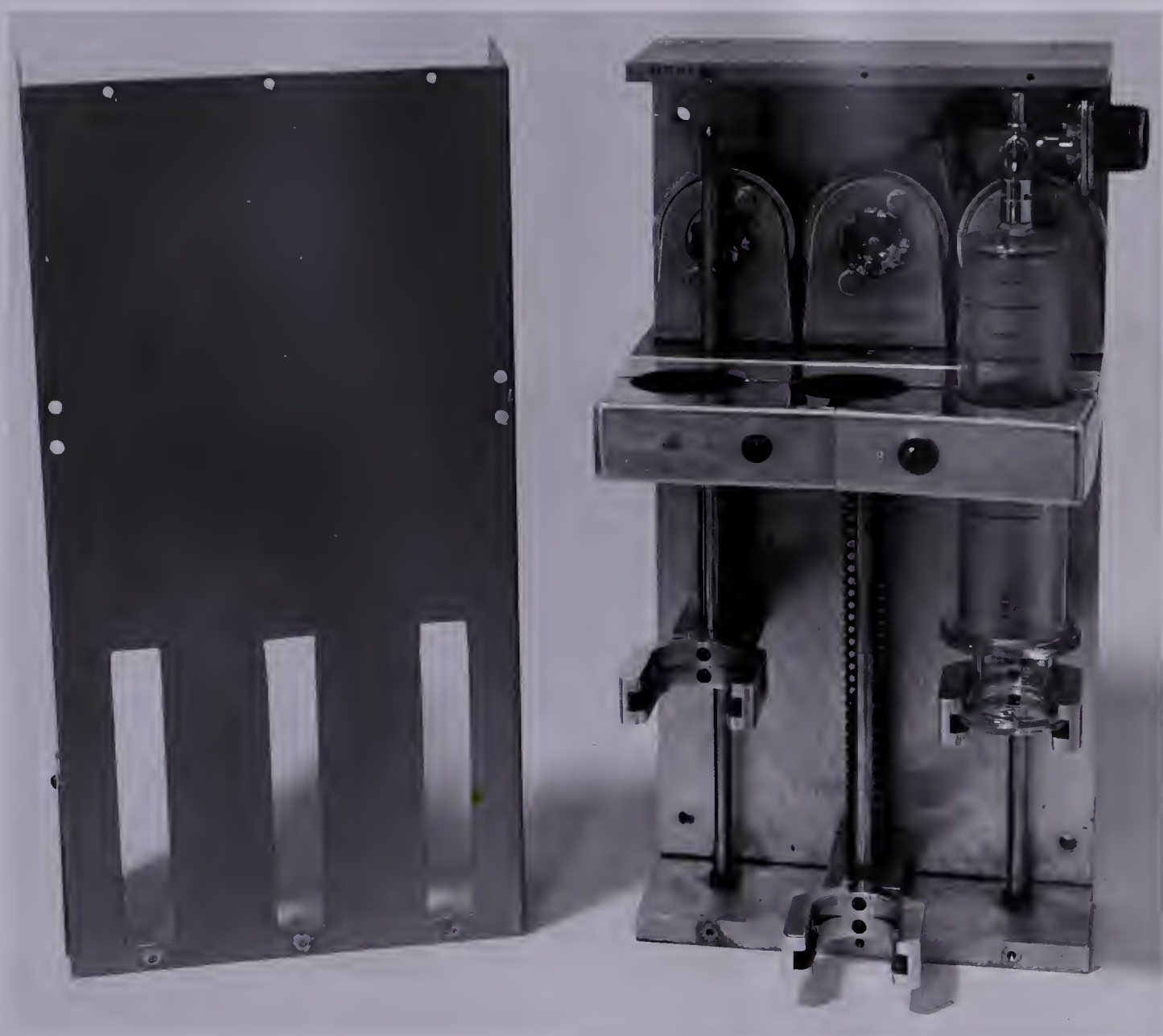
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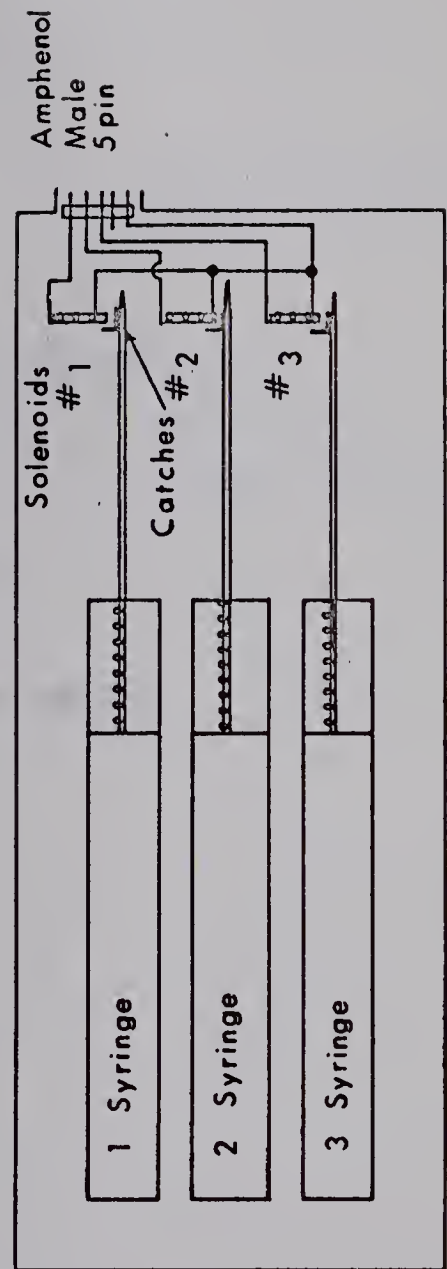
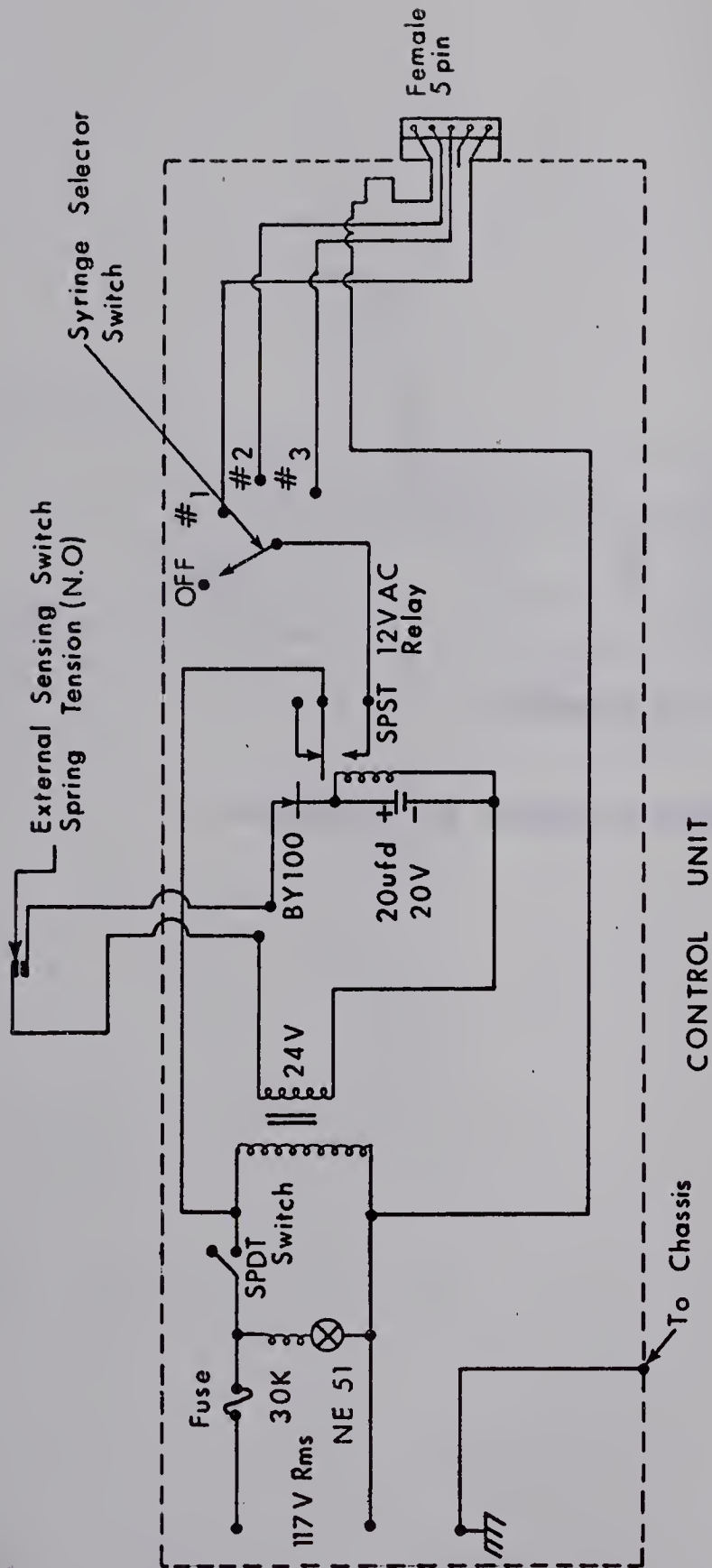
APPENDIX A

DESIGN OF THE SYRINGE SAMPLING APPARATUS



APPENDIX B

CIRCUIT DIAGRAM OF THE CONTROL UNIT FOR
THE SYRINGE SAMPLER

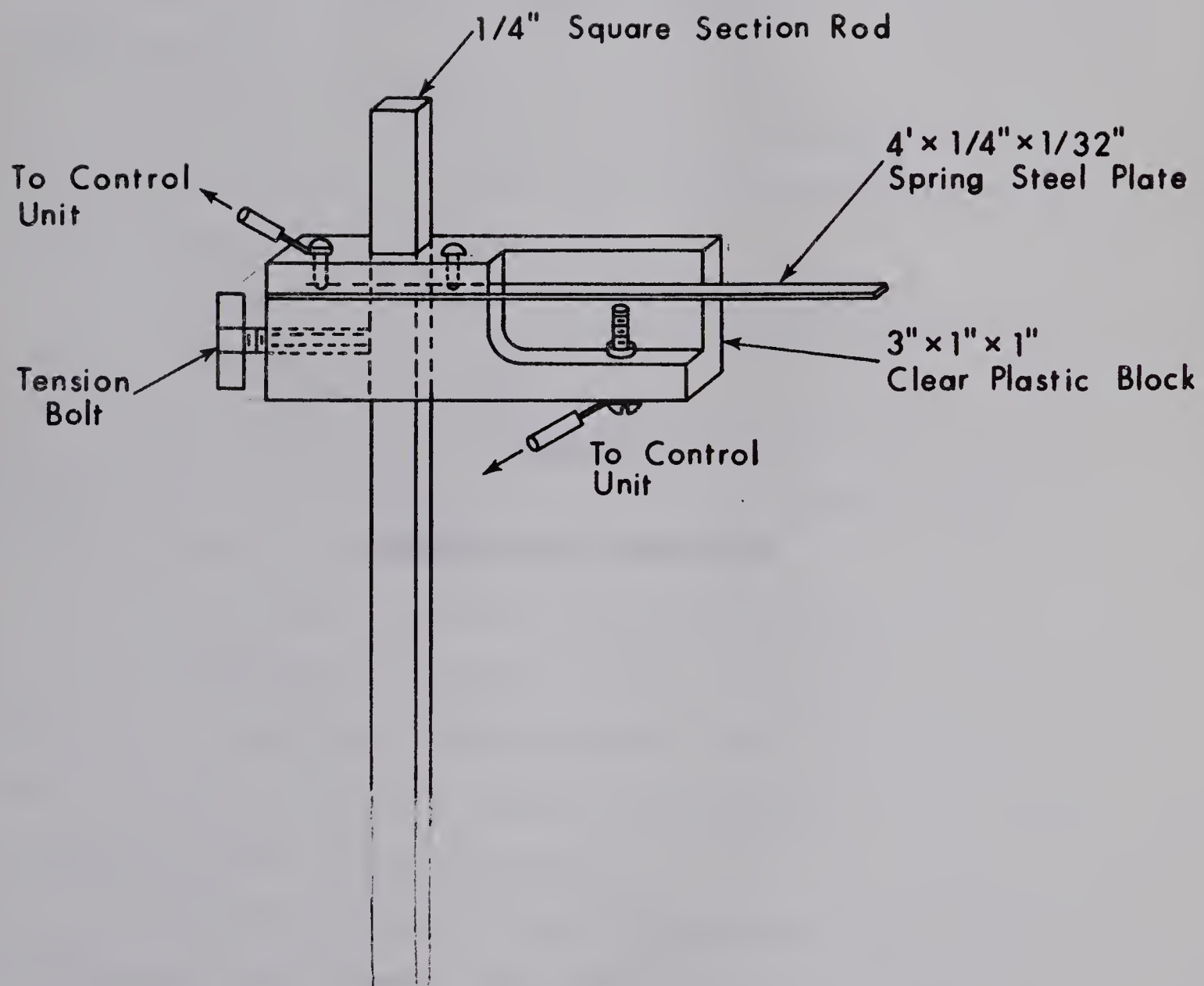


SYRINGE SAMPLER



APPENDIX C

DESIGN OF THE AUTOMATIC SAMPLING SWITCH



APPENDIX D

COMPUTER CARD PRESENTATION

COMPUTER CARD PRESENTATION

Monitor Control Cards

These cards are punched in the following manner when using the IBSYS system (23):

Column #1. A \$ sign is punched in this column on all the monitor control cards.

Columns #2-8. The Control Card Name, which may consist of from one to seven alphabetic characters, such characters to be punched on the cards, commencing in Column #2.

Columns #8-13. The Deckname Field, which may, on some cards, contain the name of the programme.

Columns #14-72. Variable Field Information. There must be no intervening blanks, as these cause the field to be terminated when the first blank space is encountered.

Columns #73-80. Reserved for serialisation purposes.

(a) \$IBSYS Card. This card is pre-punched, but additional information must be written upon it to show the job number, the programmer's name and telephone extension, the type of input material and the manner in which the output is to be presented.

(b) \$JOB Card. The title "\$JOB" is punched in Columns #1 to #4, the Deckname field is left blank, and a six digit Job Number is punched into the Variable Field Information section, commencing at column #16, after which may follow any identifying information required by the programmer.

(c) \$TIME Card. The title "\$TIME" is punched in columns #1 - #5

and the Deckname Field is left blank. An estimate of the total processing time required for the job, in minutes, is punched in the Variable Field Information section, commencing at column #16. A comma follows immediately, and an estimate of the total number of lines of output to be printed completes the information to be punched onto this card.

(d) \$IBJOB Card. The title of this card is printed in columns #1 - #6. A name may be punched in the Deckname Field in alphabetic characters, and the word "GO" should be punched at the beginning of the Variable Field Information section of this card. A blank may be included between the Deckname and the Variable Field Information.

(e) \$IBFTC Card. This card follows the cards mentioned above, and a similar card is placed at the beginning of any sub-routine. The title is punched in the appropriate column, and the Deckname Field must contain a name if there is more than one deck. In the accompanying programme, the name of the Mainline programme is "TRIAL", and as there is a sub-routine deck, this is entitled "TRIAM". This card calls the Fortran IV Compiler to process the deck that follows. The words, "NOLIST, NODECK" are then punched, as shown, commencing at column #16 on the card. This information indicates that the programmer does not require the output of the Fortran IV compiler, or the complete MAP language listing to be given. It also indicates that a binary deck is not to be punched.

(f) \$ENTRY Card. This card indicates the end of the storage load. The title is punched into the column reserved for it and no other information need follow.

This card must be placed immediately in front of the data deck

(prior to the first Subject Control Card).

Mainline Programme Deck

Columns #1 - #5 in Fortran IV programming, are reserved for statement numbers that are used for cross-referencing purposes.

If the letter "C" is punched in column #1, then the line that follows is not processed as part of the programme, but is printed on the output to provide a means of clarification or identification of the elements of the programme. Many such cards are included in the accompanying programme for explanatory purposes.

Column #6 is used to indicate a continuation card. When the programme information of a particular operation exceeds the boundaries imposed on one card, a non-zero numeral is then punched in this column of the next card, and punching of the operation continued in column #6. If the information can be fitted on one card, this column is left blank.

Columns #7-72. The statements or programming information are then punched on the cards using these columns. Blanks may be included to make the statements readable.

Columns #73-80 are not processed and may be used to identify the programme by name, and to cumulatively number the cards of the mainline programme (27).

Sub-routine Programme Deck

This deck is prepared in the same manner as the Mainline Programme, but, if columns #73-80 are used for identification purposes, the sub-routine name should be used and the cards numbered separately from those of the main programme.

Subject Control Card

One of these cards is required for each subject's data, and must precede that data. The card is prepared in the following manner:

Column #1. The output code number used in the particular computer is punched in this column. At the University of Alberta, the numeral "6" indicates a WRITE operation.

Column #2. The input code number of the particular computer is punched in this space. The University of Alberta system uses the numeral "5" for this READ a card operation.

Column #3. The number of resting trials made by the particular subject. This programme is limited to a maximum of seven trials for each subject.

Column #4. The number of exercise trials. It must be emphasized that at least four resting trials should precede the exercise trials, as the pulmonary parenchymal tissue volume must be calculated at rest, and then used in the equations of the exercise calculations.

Column #5. If the printed output is desired, a zero is punched in this column. If the full array of the sixty answers is required, punch a "1" in this column. Under normal circumstances, the printed output is the more convenient of the two to use.

Columns #6-61. The subject's name is punched in this space, and any other information that may be relevant may be included.

Columns #62-71. The date of testing is punched in this field, in the form, "2 APR 1967."

Columns #72-80. These columns may be used for identification purposes, in a code decided by the programmer.

Data Cards

Data card #1. Column #1. If the subject is male, place the numeral "1" in this column. If the subject is female, the numeral "2" is used.

Columns #2-4. The age of the subject in years is punched here, with the months expressed as a single decimal. It is emphasised that no decimal points should appear on the data cards.

Columns #5-7. The subject's weight in pounds.

Columns #8-10. The subject's height in inches, with fractions expressed as one decimal.

Columns #11-14. The height in millimeters, of the chromatogram peak of the neon in the inspiratory mixture. Fractions may be expressed as one decimal.

Columns #15-18. The area in square millimeters, of the inspired oxygen peak. This field may be left blank if so desired. There is no provision here for decimal places.

Columns #19-22. The height in millimeters of inspired nitrogen peak. This field may be left blank if desired. Fractions may be expressed as one decimal.

Columns #23-26. The height in millimeters of the inspired carbon dioxide peak. Most detectors will not record room air concentrations of carbon dioxide, and still produce a peak for the expired concentration of the gas that will fit on the recorder chart. For this reason, this field may be left blank. Fractions may be expressed as one decimal.

Columns #27-30. The height of the inspired carbon monoxide peak in millimeters, correct to one decimal place. If the researcher wishes to

calculate pulmonary capillary blood flow alone, carbon monoxide peaks need not be measured.

Columns #31-34. The height of the inspired acetylene peak in millimeters, correct to one decimal place. Acetylene measurements may be omitted if the calculation of pulmonary capillary blood flow is not required.

Columns #35-38. The height of the chromatogram peak of the expired neon, in millimeters, correct to one decimal place.

Columns #39-42. The area of the expired oxygen peak in square millimeters. There is no provision for decimals in this field. This measurement may be omitted if so desired.

Columns #43-46. The height of the expired nitrogen peak in millimeters, correct to one decimal place. This field may be left blank if so desired.

Columns #47-50. The height of the expired carbon dioxide peak in millimeters, correct to one decimal place. This field may be left blank.

Columns #51-54. The height of the expired carbon monoxide peak in millimeters, correct to one decimal place.

Columns #55-58. The height of the expired acetylene peak in millimeters, correct to one decimal place.

Columns #59-62. The volume of the special gas mixture taken into the lungs for breath-holding, expressed in milliliters. There is no provision for decimals in this field.

Columns #63-66. If it is desired to analyse diffusing capacity of the lung for carbon monoxide between two time periods in expiration,

the time of breath-holding up to the collection of the first sample should be included in this field. There is provision for the time to be measured correct to two decimal places in this field. If this measure is not required, leave this field blank.

Columns #67-70. Breath-holding time in seconds, correct to two decimal places. If sequential sampling is used, the time of breath-holding up to the collection of the second sample is included here.

Columns #75-77. The initials of the subject may be punched in these columns.

Columns #78-80. The cumulative sequence numbers of the data cards of the particular subject are punched in these columns.

Data Card #2. Columns #1-3. The barometric pressure less the pressure of water vapour in the alveolar volume of the lung (P_B-47), in millimeters of mercury, recorded at the time of the test, is included in this field. There is no provision in this field for decimals.

Columns #4-6. The correction factor to convert inspired volume to standard temperature and pressure (dry), correct to three decimal places, is included in this field.

Columns #7-9. The heart rate of the subject during the breath-holding period, converted to beats per minute. There is no provision for decimals in this field.

Columns #10-13. When performing measurements during exercise, the work load for the test is included in this field. There is no provision for decimals. For all tests performed at rest, this field may be left blank.

Columns #14-17. The concentration of oxygen in the gas cylinder used for supplying the inspiration mixture, correct to two decimal places. This measurement may be left blank if not required.

Columns #75-77. The initials of the subject tested may be punched in this space.

Columns #78-80. The cumulative sequence numbers of the particular subject's cards may be punched in this field.

Blank Card

This card should be left completely blank and placed at the rear of the combined decks.

APPENDIX E

COMPUTER PROGRAMME FOR THE CALCULATION OF DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE AND PULMONARY CAPILLARY BLOOD FLOW


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$IRSYS
$JOB          705020
$TIME        4,4000
$IRJOB PETRIE GO
$IBFTC TRIAL  NOLIST,NODECK
C *****TRIAL 1
C PROGRAMME TO CALCULATE PULMONARY CAPILLARY BLOOD FLOW (CARDIAC TRIAL 2
C OUTPUT), DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE TRIAL 3
C AND ALLIED PARAMETERS BY THE SINGLE BREATH METHOD TRIAL 4
C PROGRAMMED BY BRIAN M. PETRIE TRIAL 5
C FACULTY OF PHYSICAL EDUCATION TRIAL 6
C UNIVERSITY OF ALBERTA TRIAL 7
C APRIL 1967 TRIAL 8
C TRIAL 9
C TRIAL 10
C COPIES OF THIS PROGRAMME (ON CARDS) ARE AVAILABLE FROM THE FITNESS TRIAL 11
C RESEARCH UNIT, FACULTY OF PHYS. ED., UNIVERSITY OF ALBERTA TRIAL 12
C TRIAL 13
C ALL ANSWERS (WHERE APPROPRIATE) ARE GIVEN IN MILLILITERS, TRIAL 14
C NOT LITERS TRIAL 15
C TRIAL 16
C FOR DIFFUSING CAPACITY STUDIES, ONLY THE PEAKS OF NEON AND CARBON TRIAL 17
C MONOXIDE NEED BE MEASURED TRIAL 18
C TRIAL 19
C FOR PULMONARY CAPILLARY BLOOD FLOW STUDIES, ONLY THE PEAKS OF NEON TRIAL 20
C AND ACETYLENE NEED BE MEASURED TRIAL 21
C TRIAL 22
C EXERCISE TRIALS MUST BE ACCOMPANIED BY FOUR RESTING TRIALS SO THAT TRIAL 23
C TISSUE VOLUME MAY BE ESTABLISHED BEFORE CALCULATION OF EXERCISE TRIAL 24
C DATA TRIAL 25
C TRIAL 26
C THE SUBTRACTION (-85) FROM THE CALCULATED ALVEOLAR VOLUME ON CARD TRIAL 27
C *TRIAL 124 REFERS TO THE INSTRUMENT DEAD SPACE, AND WILL VARY TRIAL 28
C WITH EACH DESIGN OF THE APPARATUS TRIAL 29
C TRIAL 30
C IF PARAMETER NOT MEASURED LEAVE FIELD BLANK TRIAL 31
C TRIAL 32
C DO NOT TYPE DECIMAL POINTS ONTO DATA CARDS PROGRAM KNOWS LOCATION TRIAL 33
C TRIAL 34
C PLACE A BLANK CARD AT THE END OF THE DECK FOLLOWING DATA CARDS TRIAL 35
C TRIAL 36
C ANSWERS 55 - 60 AVAILABLE FOR ADDITIONAL COMPUTATIONS IF REQUIRED TRIAL 37
C *****TRIAL 38
C CONTROL CARD TRIAL 39
C COL 1 = OUTPUT DEVICE CODE (WRITE CODE NO.) (MX) TRIAL 40
C COL 2 = INPUT DEVICE CODE (READ CODE NO.) (MY) NOTE, MZ ON CARD TRIAL 41
C *TRIAL 96 MUST CONTAIN THE INPUT DEVICE CODE TO READ CONTROL TRIAL 42
C CARD TRIAL 43
C COL 3 = NO. OF REST TESTS. 7 = MAX NO. OF REST + EXERCISE TESTS TRIAL 44
C COL 4 = NO. OF EXERCISE TESTS TRIAL 45

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C      COL 5 = PRINT MATRIX CODE  0 = NO PRINT, 1 = PRINT          TRIAL 46
C      COL 6 - 61 = NAME                                           TRIAL 47
C      COL 62 - 71 = DATE                                           TRIAL 48
C      COL 73 - 80 = ID                                             TRIAL 49
C      *****TRIAL 50
C      DATA CARD *1                                              TRIAL 51
C      COL 1 = SEX (MALE = 1, FEMALE = 2)                          TRIAL 52
C      COL 2 - 4 = AGE (MONTHS EXPRESSED AS ONE DECIMAL IN COL *4) TRIAL 53
C      COL 5 - 7 = WEIGHT IN POUNDS                                TRIAL 54
C      COL 8 - 10 = HEIGHT (FRACTIONS AS ONE DECIMAL IN COL *10)   TRIAL 55
C      COL 11 - 14 = PEAK HEIGHT TANK NEON IN M.M. (ONE DECIMAL)   TRIAL 56
C      COL 15 - 18 = PEAK AREA TANK OXYGEN IN SQ. M.M. (NO DECIMALS) TRIAL 57
C      COL 19 - 22 = PEAK HEIGHT TANK NITROGEN IN M.M. (ONE DECIMAL) TRIAL 58
C      COL 23 - 26 = PEAK HEIGHT TANK CO2 IN M.M. (ONE DECIMAL)    TRIAL 59
C      COL 27 - 30 = PEAK HEIGHT TANK CO IN M.M. (ONE DECIMAL)     TRIAL 60
C      COL 31 - 34 = PEAK HEIGHT TANK ACETYLENE IN M.M. (ONE DECIMAL) TRIAL 61
C      COL 35 - 38 = PEAK HEIGHT ALVEOLAR NEON IN M.M. (ONE DECIMAL) TRIAL 62
C      COL 39 - 42 = PEAK AREA ALV. OXYGEN IN SQ. M.M. (NO DECIMALS) TRIAL 63
C      COL 43 - 46 = PEAK HEIGHT ALV. NITROGEN IN M.M. (ONE DECIMAL) TRIAL 64
C      COL 47 - 50 = PEAK HEIGHT ALV. CO2 IN M.M. (ONE DECIMAL)    TRIAL 65
C      COL 51 - 54 = PEAK HEIGHT ALV. CO IN M.M. (ONE DECIMAL)     TRIAL 66
C      COL 55 - 58 = PEAK HEIGHT ALV. ACETYLENE IN M.M. (ONE DECIMAL) TRIAL 67
C      COL 59 - 62 = INSPIRED VOLUME IN M.L. (NO DECIMALS)        TRIAL 68
C      COL 63 - 66 = TIME *1 IN SECONDS, IF REQUIRED (TWO DECIMALS) TRIAL 69
C      COL 67 - 70 = BREATH HOLDING TIME IN SECONDS (TWO DECIMALS) TRIAL 70
C      COL 75 - 77 = SUBJECT OR PATIENTS INITIALS                 TRIAL 71
C      COL 78 - 80 = SEQUENCE NUMBERS FOR ORDERING CARDS          TRIAL 72
C      *****TRIAL 73
C      DATA CARD *2                                              TRIAL 74
C      COL 1 - 3 = BAROMETRIC PRESSURE LESS PH2O (PB-47) IN M.M. HG. TRIAL 75
C      COL 4 - 6 = STPD FACTOR (THREE DECIMALS)                   TRIAL 76
C      COL 7 - 9 = HEART RATE (NO DECIMALS)                       TRIAL 77
C      COL 10 - 13 = WORK LOAD (FOR EXERCISE) (NO DECIMALS)       TRIAL 78
C      COL 14 - 17 = OXYGEN CONC. IN REFERENCE TANK (TWO DECIMALS) TRIAL 79
C      COL 75 - 77 = SUBJECT OR PATIENTS INITIALS                 TRIAL 80
C      COL 78 - 80 = SEQUENCE NUMBERS FOR ORDERING CARDS          TRIAL 81
C      *****TRIAL 82
C      TRIAL 83
C      INTEGER DATE(5)                                           TRIAL 84
C      DIMENSION S(8)                                           TRIAL 85
C      COMMON DATE,NAME(28),ANS(8,60),MX,MY,NOSUB                TRIAL 86
C      EQUIVALENCE(S(1),SYA),(S(2),SYB),(S(3),SY2A),(S(4),SY2B),(S(5),SXY TRIAL 87
C      1A),(S(6),SXYB),(S(7),SXA,SXB),(S(8),SX2A,SX2B)           TRIAL 88
C      TRIAL 89
100    FORMAT(5I1,28A2,5A2)                                       TRIAL 90
102    FORMAT(I1,F3.1,F3.0,F3.1,F4.1,F4.0,5F4.1,F4.0,4F4.1,F4.0,2F4.2) TRIAL 91
103    FORMAT(F3.0,F3.3,F3.0,F4.0,F4.2)                          TRIAL 92
104    FORMAT(1X,I10,4E16.8)                                       TRIAL 93
105    FORMAT(1H1)                                                 TRIAL 94
106    FORMAT(1HL)                                                 TRIAL 95

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2 MZ=5 TRIAL 96
  READ(MZ,100) MX,MY,ITRYR,ITRYX,ITABL,(NAME(I),I=1,28),(DATE(I),I=1 TRIAL 97
1,5) TRIAL 98
  IF (MX) 68,68,4 TRIAL 99
4 NTEST=ITRYR+ITRYX TRIAL100
  TRYR=ITRYR TRIAL101
  TRYX=ITRYX TRIAL102
  NOSUB=1 TRIAL103
  ITEST=0 TRIAL104
  IBOX=0 TRIAL105
  DO 6 I=1,8 TRIAL106
6 S(I)=0. TRIAL107
  DO 8 J=1,60 TRIAL108
  DO 8 I=1,8 TRIAL109
8 ANS(I,J)=0. TRIAL110
10 ITEST=ITEST+1 TRIAL111
  READ(MY,102) ISEX,AGE,ANS(8,1),ANS(8,2),BNEON,BO2,BN2,BCO2,BCO,BA,ATRIAL112
1NEON,AO2,AN2,ACO2,ACO,AA,VOL,T1,T2 TRIAL113
  READ(MY,103) (ANS(ITEST,M),M=3,6),TO2 TRIAL114
  ANS(8,7)=(((ANS(8,1)*.4536)**.425)*((ANS(8,2)*2.54)**.725))*0.00718 TRIAL115
14 TRIAL116
C TRIAL117
C ANSWER 8,7 = BODY SURFACE AREA (BSA) TRIAL118
C TRIAL119
C ANS(ITEST,8)=VOL*ANS(ITEST,4) TRIAL120
C TRIAL121
C ANSWER 8 = INSPIRED VOLUME STPD (VI STPD) TRIAL122
C TRIAL123
C ANS(ITEST,9)=(ANS(ITEST,8)*BNEON/ANFON)-85. TRIAL124
C TRIAL125
C ANSWER 9 = ALVEOLAR VOLUME (VA) TRIAL126
C TRIAL127
C ANS(ITEST,10)=ANS(ITEST,9)-ANS(ITEST,8) TRIAL128
C TRIAL129
C ANSWER 10 = RESIDUAL VOLUME STPD (RV STPD) TRIAL130
C TRIAL131
C ANS(ITEST,11)=ANS(ITEST,10)*1.21 TRIAL132
C TRIAL133
C ANSWER 11 = RESIDUAL VOLUME BTPS (RV BTPS) TRIAL134
C TRIAL135
C ANS(ITEST,12)=ANEON/BNEON TRIAL136
C TRIAL137
C ANSWER 12 = ALVEOLAR / BAG NEON TRIAL138
C TRIAL139
C ANS(ITEST,13)=ANS(ITEST,12)*BCO TRIAL140
C TRIAL141
C ANSWER 13 = INITIAL CARBON MONOXIDE (CO O) TRIAL142
C TRIAL143
C ANS(ITEST,14)=ANS(ITEST,12)*BA TRIAL144
C TRIAL145

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C	ANSWER 14 = INITIAL ACETYLENE (C ₂ H ₂ O)	TRIAL146
C		TRIAL147
	ANS(ITEST,15)=ACO/ANS(ITEST,13)	TRIAL148
C		TRIAL149
C	ANSWER 15 = ALVEOLAR / INITIAL CARBON MONOXIDE	TRIAL150
C		TRIAL151
	ANS(ITEST,16)=AA/ANS(ITEST,14)	TRIAL152
C		TRIAL153
C	ANSWER 16 = ALVEOLAR / INITIAL ACETYLENE	TRIAL154
C		TRIAL155
	ANS(ITEST,17)=ANS(ITEST,13)/ACO	TRIAL156
C		TRIAL157
C	ANSWER 17 = INITIAL / ALVEOLAR CARBON MONOXIDE	TRIAL158
C		TRIAL159
	ANS(ITEST,18)=ANS(ITEST,14)/AA	TRIAL160
C		TRIAL161
C	ANSWER 18 = INITIAL / ALVEOLAR ACETYLENE	TRIAL162
C		TRIAL163
	ANS(ITEST,19)=T2-T1	TRIAL164
C		TRIAL165
C	ANSWER 19 = BREATH HOLDING TIME	TRIAL166
C		TRIAL167
	ANS(ITEST,20)=T02*AO2/BO2	TRIAL168
C		TRIAL169
C	ANSWER 20 = ALVEOLAR OXYGEN CONCENTRATION (FO ₂)	TRIAL170
C		TRIAL171
	ANS(ITEST,21)=ANS(ITEST,20)*ANS(1,3)/100.	TRIAL172
C		TRIAL173
C	ANSWER 21 = PARTIAL PRESSURE OF OXYGEN (PAO ₂)	TRIAL174
C		TRIAL175
	IBOX=IBOX+1	TRIAL176
	IF (IBOX/NTEST.EQ.1) GO TO 12	TRIAL177
	GO TO 10	TRIAL178
12	CONTINUE	TRIAL179
14	DO 16 I=1,ITRYR	TRIAL180
	ANS(8,20)=ANS(8,20)+ANS(I,20)/TRYR	TRIAL181
	ANS(8,21)=ANS(8,21)+ANS(I,21)/TRYR	TRIAL182
16	ANS(8,24)=ANS(8,24)+ANS(I,9)/TRYR	TRIAL183
C		TRIAL184
C	ANSWER 8,24 = AVERAGE RESTING ALVEOLAR VOLUME STPD (VA STPD AVGE)	TRIAL185
C		TRIAL186
	DO 20 I=1,ITRYR	TRIAL187
	ANS(I,25)=ANS(8,24)*60./ANS(I,3)	TRIAL188
	ANS(I,26)=ANS(I,25)/ANS(I,19)	TRIAL189
	ANS(I,27)=ALOG(ANS(I,17))	TRIAL190
	ANS(I,28)=ANS(I,26)*ANS(I,27)	TRIAL191
C		TRIAL192
C	ANSWER 28 = DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE	TRIAL193
C		TRIAL194
	DO 18 K=1,2	TRIAL195

	S(K)=ALOG10(ANS(I,K+14))+S(K)	TRIAL196
	S(K+2)=ALOG10(ANS(I,K+14))**2+S(K+2)	TRIAL197
18	S(K+4)=ANS(I,19)*ALOG10(ANS(I,K+14))+S(K+4)	TRIAL198
	S(7)=ANS(I,19)+S(7)	TRIAL199
	S(8)=ANS(I,19)**2+S(8)	TRIAL200
20	CONTINUE	TRIAL201
	ANS(8,29)=(SXYA*TRYR-SXA*SYA)/(SX2A*TRYR-SXA**2)	TRIAL202
C		TRIAL203
C	ANSWER 29 = BETA SLOPE OF CARBON MONOXIDE DISAPPEARANCE	TRIAL204
C		TRIAL205
	ANS(8,30)=SYA/TRYR-ANS(8,29)*SXA/TRYR	TRIAL206
	ANS(8,30)=10.**(ANS(8,30))	TRIAL207
C		TRIAL208
C	ANSWER 30 = ALPHA INTERCEPT OF CARBON MONOXIDE DISAPPEARANCE	TRIAL209
C		TRIAL210
	ANS(8,31)=13816./ANS(1,3)	TRIAL211
	ANS(8,32)=ANS(8,31)*(ANS(8,24)/1000.)	TRIAL212
	Y2A=(ALOG10(ANS(8,30)))+(ANS(8,29)*2.)	TRIAL213
	Y12A=(ALOG10(ANS(8,30)))+(ANS(8,29)*12.)	TRIAL214
	ANS(8,33)=ALOG10(10.**Y2A/10.**Y12A)	TRIAL215
	ANS(8,28)=ANS(8,32)*ANS(8,33)	TRIAL216
C		TRIAL217
C	ANSWER 8,28 = DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE	TRIAL218
C		TRIAL219
	ANS(8,34)=(SXYB*TRYR-SXB*SYB)/(SX2B*TRYR-SXB**2)	TRIAL220
C		TRIAL221
C	ANSWER 34 = BETA SLOPE OF ACETYLENE DISAPPEARANCE	TRIAL222
C		TRIAL223
	ANS(8,35)=SYB/TRYR-ANS(8,34)*SXB/TRYR	TRIAL224
	ANS(8,35)=10.**(ANS(8,35))	TRIAL225
C		TRIAL226
C	ANSWER 35 = ALPHA INTERCEPT OF ACETYLENE DISAPPEARANCE	TRIAL227
C		TRIAL228
	ANS(8,36)=ANS(8,24)/.768	TRIAL229
	ANS(8,37)=ANS(8,35)*100.	TRIAL230
	ANS(8,38)=(100./ANS(8,37))-1.	TRIAL231
	ANS(8,39)=760./ANS(1,3)	TRIAL232
	ANS(8,40)=ANS(8,36)*ANS(8,38)*ANS(8,39)	TRIAL233
C		TRIAL234
C	ANSWER 40 = TISSUE VOLUME OF THE LUNG (VT)	TRIAL235
C		TRIAL236
	ANS(8,41)=ANS(8,24)/(ANS(8,24)+.768*ANS(8,40))	TRIAL237
	ANS(8,42)=ANS(8,41)*.740*ANS(1,3)	TRIAL238
	ANS(8,43)=ANS(8,24)*760.*60.	TRIAL239
	DO 22 I=1,ITRYR	TRIAL240
	ANS(I,44)=ANS(8,43)/(ANS(8,42)*ANS(I,19))	TRIAL241
	ANS(I,45)=ALOG(ANS(8,41)*ANS(I,18))	TRIAL242
	ANS(I,46)=ANS(I,44)*ANS(I,45)	TRIAL243
22	ANS(8,46)=ANS(I,46)/TRYR+ANS(8,46)	TRIAL244
C		TRIAL245

C	ANSWER 46 = PULMONARY CAPILLARY BLOOD FLOW - CARDIAC OUTPUT	TRIAL246
C		TRIAL247
24	IF(ITRYX) 30,30,26	TRIAL248
26	K=ITRYR+1	TRIAL249
	DO 28 I=K,NTEST	TRIAL250
	ANS(I,25)=ANS(I,9)*60./ANS(I,3)	TRIAL251
	ANS(I,26)=ANS(I,25)/ANS(I,19)	TRIAL252
	ANS(I,27)=ALOG(ANS(I,17))	TRIAL253
	ANS(I,28)=ANS(I,26)*ANS(I,27)	TRIAL254
C		TRIAL255
C	ANSWER 28 = DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE	TRIAL256
C		TRIAL257
	ANS(I,41)=ANS(I,9)/(ANS(I,9)+.768*ANS(8,40))	TRIAL258
	ANS(I,42)=ANS(I,41)*ANS(I,27)	TRIAL259
	ANS(I,43)=ANS(I,19)*760.*60.	TRIAL260
	ANS(I,44)=ANS(I,43)/(ANS(I,42)*ANS(I,19))	TRIAL261
	ANS(I,45)=ALOG(ANS(I,41)*ANS(I,18))	TRIAL262
	ANS(I,46)=ANS(I,44)*ANS(I,45)	TRIAL263
C		TRIAL264
C	ANSWER 46 = PULMONARY CAPILLARY BLOOD FLOW - CARDIAC OUTPUT	TRIAL265
C		TRIAL266
28	ANS(I,50)=ANS(I,46)/ANS(I,6)	TRIAL267
C		TRIAL268
C	ANSWER 50 = CARDIAC OUTPUT / WORK LOAD	TRIAL269
C		TRIAL270
30	CONTINUE	TRIAL271
32	DO 34 I=1,NTEST	TRIAL272
	ANS(I,47)=ANS(I,46)/ANS(I,5)	TRIAL273
C		TRIAL274
C	ANSWER 47 = STROKE VOLUME (SV)	TRIAL275
C		TRIAL276
	ANS(I,48)=ANS(I,47)/ANS(8,7)	TRIAL277
C		TRIAL278
C	ANSWER 48 = STROKE INDEX (SI)	TRIAL279
C		TRIAL280
34	ANS(I,49)=ANS(I,46)/ANS(8,7)	TRIAL281
C		TRIAL282
C	ANSWER 49 = CARDIAC INDEX (CI)	TRIAL283
C		TRIAL284
	ANS(8,51)=.01934*(ANS(8,2)**3)	TRIAL285
C		TRIAL286
C	ANSWER 8,51 = PREDICTED TOTAL LUNG CAPACITY (PTLC) FOR MALES	TRIAL287
C		TRIAL288
	ANS(8,53)=25.-(0.117*AGE)	TRIAL289
C		TRIAL290
C	ANSWER 8,53 = PREDICTED DIFFUSING CAPACITY (PDLCO) FOR MALES	TRIAL291
C		TRIAL292
	GO TO (38,36),ISEX	TRIAL293
36	ANS(8,51)=.01803*(ANS(8,2)**3)	TRIAL294
C		TRIAL295

C	ANSWER 8,51 = PREDICTED TOTAL LUNG CAPACITY (PTLC) FOR FEMALES	TRIAL296
C		TRIAL297
	$ANS(8,53)=15.5*ANS(8,7)-(.117*AGE)-.5$	TRIAL298
C		TRIAL299
C	ANSWER 8,53 = PREDICTED DIFFUSING CAPACITY (PDLCO) FOR FEMALES	TRIAL300
C		TRIAL301
	38 $ANS(8,52)=ANS(8,51)*.1417$	TRIAL302
C		TRIAL303
C	ANSWER 8,52 = PREDICTED TISSUE VOLUME (PVT)	TRIAL304
C		TRIAL305
	40 $ANS(8,54)=ANS(8,7)*3100.$	TRIAL306
C		TRIAL307
C	ANSWER 8,54 = PREDICTED CARDIAC OUTPUT	TRIAL308
C		TRIAL309
	48 CONTINUE	TRIAL310
	50 IF (ITABL) 66,66,52	TRIAL311
	52 WRITE(MX,105)	TRIAL312
	DO 56 J=1,20	TRIAL313
	IF (J.GT.1) GO TO 54	TRIAL314
	WRITE(MX,106)	TRIAL315
	54 WRITE(MX,104)J,(ANS(I,J),I=1,4)	TRIAL316
	56 WRITE(MX,104)J,(ANS(I,J),I=5,8)	TRIAL317
	WRITE(MX,105)	TRIAL318
	DO 60 J=21,40	TRIAL319
	IF (J.GT.21) GO TO 58	TRIAL320
	WRITE(MX,106)	TRIAL321
	58 WRITE(MX,104)J,(ANS(I,J),I=1,4)	TRIAL322
	60 WRITE(MX,104)J,(ANS(I,J),I=5,8)	TRIAL323
	WRITE(MX,105)	TRIAL324
	DO 64 J=41,60	TRIAL325
	IF (J.GT.41) GO TO 62	TRIAL326
	WRITE(MX,106)	TRIAL327
	62 WRITE(MX,104)J,(ANS(I,J),I=1,4)	TRIAL328
	64 WRITE(MX,104)J,(ANS(I,J),I=5,8)	TRIAL329
	GO TO 2	TRIAL330
	66 CALL TRIAM	TRIAL331
	GO TO 2	TRIAL332
	68 STOP	TRIAL333
C		TRIAL334
C	ANSWER 8,1 = WEIGHT	TRIAL335
C	ANSWER 8,2 = HEIGHT	TRIAL336
C	ANSWER 3 = BAROMETRIC PRESSURE - WATER PRESSURE (PB - PH2O)	TRIAL337
C	ANSWER 4 = STPD FACTOR	TRIAL338
C	ANSWER 5 = HEART RATE	TRIAL339
C	ANSWER 6 = EXERCISE WORK LOAD	TRIAL340
C	ANSWER 8,7 = BODY SURFACE AREA (RSA)	TRIAL341
C	ANSWER 8 = INSPIRED VOLUME STPD (VI STPD)	TRIAL342
C	ANSWER 9 = ALVEOLAR VOLUME (VA)	TRIAL343
C	ANSWER 10 = RESIDUAL VOLUME STPD (RV STPD)	TRIAL344
C	ANSWER 11 = RESIDUAL VOLUME BTPS (RV BTPS)	TRIAL345

C	ANSWER 12 = ALVEOLAR / RAG NEON	TRIAL346
C	ANSWER 13 = INITIAL CARBON MONOXIDE (CO O)	TRIAL347
C	ANSWER 14 = INITIAL ACETYLENE (C2H2 O)	TRIAL348
C	ANSWER 15 = ALVEOLAR / INITIAL CARBON MONOXIDE	TRIAL349
C	ANSWER 16 = ALVEOLAR / INITIAL ACETYLENE	TRIAL350
C	ANSWER 17 = INITIAL / ALVEOLAR CARBON MONOXIDE	TRIAL351
C	ANSWER 18 = INITIAL / ALVEOLAR ACETYLENE	TRIAL352
C	ANSWER 19 = BREATH HOLDING TIME	TRIAL353
C	ANSWER 20 = ALVEOLAR OXYGEN CONCENTRATION (FO2)	TRIAL354
C	ANSWER 21 = PARTIAL PRESSURE OF OXYGEN (PAO2)	TRIAL355
C	ANSWER 8,24 = AVERAGE RESTING ALVEOLAR VOLUME STPD (VA STPD AVGE)	TRIAL356
C	ANSWER 25 = $VA*60 / (PB-47)$	TRIAL357
C	ANSWER 26 = $(VA*60/(PB-47))/(1/TIME)$	TRIAL358
C	ANSWER 27 = NATURAL LOG OF INITIAL / ALVEOLAR CARBON MONOXIDE	TRIAL359
C	ANSWER 28 = DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE	TRIAL360
C	ANSWER 29 = BETA SLOPE OF CARBON MONOXIDE DISAPPEARANCE	TRIAL361
C	ANSWER 30 = ALPHA INTERCEPT OF CARBON MONOXIDE DISAPPEARANCE	TRIAL362
C	ANSWER 8,31 = $13816 / (PB-47)$	TRIAL363
C	ANSWER 32 = $(13816/(PB-47))*VA$ (IN LITERS)	TRIAL364
C	ANSWER 8,33 = LOG OF THE SLOPE OF CARBON MONOXIDE DISAPPEARANCE	TRIAL365
C	ANSWER 34 = BETA SLOPE OF ACETYLENE DISAPPEARANCE	TRIAL366
C	ANSWER 35 = ALPHA INTERCEPT OF ACETYLENE DISAPPEARANCE	TRIAL367
C	ANSWER 8,36 = $VA/ALPHA T$	TRIAL368
C	ANSWER 8,37 = ACETYLENE INTERCEPT EXPRESSED AS PERCENTAGE	TRIAL369
C	ANSWER 8,38 = $(100/ACETYLENE INTERCEPT IN PERCENT)-1$	TRIAL370
C	ANSWER 8,39 = $760/(PB-47)$	TRIAL371
C	ANSWER 40 = TISSUE VOLUME OF THE LUNG (VT)	TRIAL372
C	ANSWER 41 = $VA/(VA+ALPHA T*TISSUE VOLUME)$	TRIAL373
C	ANSWER 42 = $ALPHA B*(VA/VA+ALPHA T*VT)*(PB-47)$	TRIAL374
C	ANSWER 43 = $VA*760*60$	TRIAL375
C	ANSWER 44 = $(VA*760*60)/ALPHA B*(VA/VA+ALPHA T*VT)*(PB-47)*B.H.TIME$	TRIAL376
C	ANSWER 45 = NATURAL LOG $((VA/VA+ALPHA T*VT)*INIT/ALV ACETYLENE)$	TRIAL377
C	ANSWER 46 = PULMONARY CAPILLARY BLOOD FLOW - CARDIAC OUTPUT	TRIAL378
C	ANSWER 47 = STROKE VOLUME (SV)	TRIAL379
C	ANSWER 48 = STROKE INDEX (SI)	TRIAL380
C	ANSWER 49 = CARDIAC INDEX (CI)	TRIAL381
C	ANSWER 50 = CARDIAC OUTPUT / WORK LOAD	TRIAL382
C	ANSWER 8,51 = PREDICTED TOTAL LUNG CAPACITY (PTLC)	TRIAL383
C	ANSWER 8,52 = PREDICTED TISSUE VOLUME (PVT)	TRIAL384
C	ANSWER 8,53 = PREDICTED DIFFUSING CAPACITY (PDLCO)	TRIAL385
C	ANSWER 8,54 = PREDICTED CARDIAC OUTPUT	TRIAL386
C		TRIAL387
	END	TRIAL388

\$IBFTC TRIAM NOLIST,NODECK

SUBROUTINE TRIAM

INTEGER DATE(5)

COMMON DATE,NAME(28),ANS(8,60),MX,MY,NOSUB

WRITE(MX,198)

198 FORMAT(1H1)

TRIAM 1

TRIAM 2

TRIAM 3

TRIAM 4

TRIAM 5

WRITE(MX,200)	TRIAM 6
200 FORMAT(1X,102HSINGLE BREATH TECHNIQUE TO OBTAIN DIFFUSING CAPACITY	TRIAM 7
1 OF LUNG FOR CO AND PULMONARY CAPILLARY BLOOD FLOW)	TRIAM 8
WRITE(MX,201)(NAME(I),I=1,28),(DATE(I),I=1,5)	TRIAM 9
201 FORMAT(1X,8HDATA OF ,28A2,6HTAKEN ,5A2)	TRIAM 10
WRITE(MX,202) ANS(8,7)	TRIAM 11
202 FORMAT(1X,23HBODY SURFACE AREA (BSA),96X	TRIAM 12
1 ,F12.4)	TRIAM 13
WRITE(MX,203)(ANS(I,8),I=1,7)	TRIAM 14
203 FORMAT(1X,30HINSPIRED VOLUME STPD (VI STPD)	TRIAM 15
1 , /7(F12.4))	TRIAM 16
WRITE(MX,204)(ANS(I,9),I=1,7)	TRIAM 17
204 FORMAT(1X,30HALVEOLAR VOLUME STPD (VA STPD)	TRIAM 18
1 , /7(F12.4))	TRIAM 19
WRITE(MX,205)(ANS(8,24))	TRIAM 20
205 FORMAT(1X,51HAVERAGE RESTING ALVEOLAR VOLUME STPD (VA STPD AVGE),6	TRIAM 21
18X ,F12.4)	TRIAM 22
WRITE(MX,206)(ANS(I,10),I=1,7)	TRIAM 23
206 FORMAT(1X,35HRESIDUAL VOLUME STPD (RV STPD NEON)	TRIAM 24
1 , /7(F12.4))	TRIAM 25
WRITE(MX,207)(ANS(I,11),I=1,7)	TRIAM 26
207 FORMAT(1X,35HRESIDUAL VOLUME RTPS (RV RTPS NEON)	TRIAM 27
1 , /7(F12.4))	TRIAM 28
WRITE(MX,208)(ANS(I,13),I=1,7)	TRIAM 29
208 FORMAT(1X,30HINITIAL CARBON MONOXIDE (CO O)	TRIAM 30
1 , /7(F12.4))	TRIAM 31
WRITE(MX,209)(ANS(I,14),I=1,7)	TRIAM 32
209 FORMAT(1X,26HINITIAL ACETYLENE (C2H2 O)	TRIAM 33
1 , /7(F12.4))	TRIAM 34
WRITE(MX,210)(ANS(I,15),I=1,7)	TRIAM 35
210 FORMAT(1X,34HALVEOLAR / INITIAL CARBON MONOXIDE	TRIAM 36
1 , /7(F12.4))	TRIAM 37
WRITE(MX,211)(ANS(I,16),I=1,7)	TRIAM 38
211 FORMAT(1X,28HALVEOLAR / INITIAL ACETYLENE	TRIAM 39
1 , /7(F12.4))	TRIAM 40
WRITE(MX,212)(ANS(I,19),I=1,7)	TRIAM 41
212 FORMAT(1X,19HBREATH HOLDING TIME	TRIAM 42
1 , /7(F12.4))	TRIAM 43
WRITE(MX,213)(ANS(8,20),(ANS(I,20),I=1,7))	TRIAM 44
213 FORMAT(1X,35HALVEOLAR OXYGEN CONCENTRATION (FO2),84X	TRIAM 45
1 ,F12.4/7(F12.4))	TRIAM 46
WRITE(MX,214)(ANS(8,21),(ANS(I,21),I=1,7))	TRIAM 47
214 FORMAT(1X,33HPARTIAL PRESSURE OF OXYGEN (PAO2),86X	TRIAM 48
1 ,F12.4/7(F12.4))	TRIAM 49
WRITE(MX,215)(ANS(8,28),(ANS(I,28),I=1,7))	TRIAM 50
215 FORMAT(1X,57HDIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE (D	TRIAM 51
1LCO),62X ,F12.4/7(F12.4))	TRIAM 52
WRITE(MX,216)(ANS(8,29))	TRIAM 53
216 FORMAT(1X,43HBETA SLOPE OF CARBON MONOXIDE DISAPPEARANCE,76X	TRIAM 54
1 ,F12.4)	TRIAM 55

WRITE(MX,217)(ANS(8,30))	TRIAM 56
217 FORMAT(1X,48HALPHA INTERCEPT OF CARBON MONOXIDE DISAPPEARANCE,71X	TRIAM 57
1 ,F12.4)	TRIAM 58
WRITE(MX,218)(ANS(8,34))	TRIAM 59
218 FORMAT(1X,37HBETA SLOPE OF ACETYLENE DISAPPEARANCE,82X	TRIAM 60
1 ,F12.4)	TRIAM 61
WRITE(MX,219)(ANS(8,35))	TRIAM 62
219 FORMAT(1X,42HALPHA INTERCEPT OF ACETYLENE DISAPPEARANCE,77X	TRIAM 63
1 ,F12.4)	TRIAM 64
WRITE(MX,220)(ANS(8,40))	TRIAM 65
220 FORMAT(1X,30HTISSUE VOLUME OF THE LUNG (VT),89X	TRIAM 66
1 ,F12.4)	TRIAM 67
WRITE(MX,221)(ANS(8,46),(ANS(I,46),I=1,7))	TRIAM 68
221 FORMAT(1X,35HPULMONARY CAPILLARY BLOOD FLOW (QC),84X	TRIAM 69
1 ,F12.4/7(F12.4))	TRIAM 70
WRITE(MX,222)(ANS(I,47),I=1,7)	TRIAM 71
222 FORMAT(1X,18HSTROKE VOLUME (SV)	TRIAM 72
1 , /7(F12.4))	TRIAM 73
WRITE(MX,223)(ANS(I,48),I=1,7)	TRIAM 74
223 FORMAT(1X,17HSTROKE INDEX (SI)	TRIAM 75
1 , /7(F12.4))	TRIAM 76
WRITE(MX,224)(ANS(I,49),I=1,7)	TRIAM 77
224 FORMAT(1X,18HCARDIAC INDFX (CI)	TRIAM 78
1 , /7(F12.4))	TRIAM 79
WRITE(MX,225)(ANS(I,50),I=1,7)	TRIAM 80
225 FORMAT(1X,35HCARDIAC OUTPUT / WORK LOAD	TRIAM 81
1 , /7(F12.4))	TRIAM 82
WRITE(MX,226)(ANS(8,51))	TRIAM 83
226 FORMAT(1X,36HPREDICTED TOTAL LUNG CAPACITY (PTLC),83X	TRIAM 84
1 ,F12.4)	TRIAM 85
WRITE(MX,227)(ANS(8,52))	TRIAM 86
227 FORMAT(1X,29HPREDICTED TISSUE VOLUME (PVT),90X	TRIAM 87
1 ,F12.4)	TRIAM 88
WRITE(MX,228)(ANS(8,53))	TRIAM 89
228 FORMAT(1X,37HPREDICTED DIFFUSING CAPACITY (PDL CO),82X	TRIAM 90
1 ,F12.4)	TRIAM 91
WRITE(MX,229)(ANS(8,54))	TRIAM 92
229 FORMAT(1X,30HPREDICTED CARDIAC OUTPUT (PCO),89X	TRIAM 93
1 ,F12.4)	TRIAM 94
RETURN	TRIAM 95
END	TRIAM 96
\$ENTRY	

1	0.	0.	0.	0.
1	0.	0.	0.	0.14000000E 03
2	0.	0.	0.	0.
2	0.	0.	0.	0.67500000E 02
3	0.65000000E 03	0.65000000E 03	0.65000000E 03	0.65000000E 03
3	0.65000000E 03	0.65000000E 03	0.65000000E 03	0.
4	0.81600000E 00	0.81600000E 00	0.81600000E 00	0.81600000E 00
4	0.81600000E 00	0.81600000E 00	0.81600000E 00	0.
5	0.70000000E 02	0.66000000E 02	0.85000000E 02	0.87000000E 02
5	0.11700000E 03	0.14200000E 03	0.16100000E 03	0.
6	0.	0.	0.	0.
6	0.60000000E 03	0.80000000E 03	0.10000000E 04	0.
7	0.	0.	0.	0.
7	0.	0.	0.	0.17470546E 01
8	0.27156480E 04	0.27303360E 04	0.27148320E 04	0.27156480E 04
8	0.27172800E 04	0.27140160E 04	0.27156480E 04	0.
9	0.40309040E 04	0.40531655E 04	0.41623983E 04	0.40962357E 04
9	0.40658057E 04	0.40937230E 04	0.40309040E 04	0.
10	0.13152559E 04	0.13228295E 04	0.14475663E 04	0.13805877E 04
10	0.13485257E 04	0.13797070E 04	0.13152559E 04	0.
11	0.15914597E 04	0.16006236E 04	0.17515553E 04	0.16705111E 04
11	0.16317160E 04	0.16694454E 04	0.15914597E 04	0.
12	0.65979381E 00	0.65979381E 00	0.63917525E 00	0.64948453E 00
12	0.65463917E 00	0.64948453E 00	0.65979381E 00	0.
13	0.11348453E 03	0.11348453E 03	0.10993814E 03	0.11171134E 03
13	0.11259794E 03	0.11171134E 03	0.11348453E 03	0.
14	0.67298968E 02	0.67298968E 02	0.65195875E 02	0.66247422E 02
14	0.66773196E 02	0.66247422E 02	0.67298968E 02	0.
15	0.81068315E 00	0.81068315E 00	0.54576144E 00	0.52814692E 00
15	0.69273028E 00	0.68032485E 00	0.66088300E 00	0.
16	0.83210785E 00	0.83210785E 00	0.73624289E 00	0.73210397E 00
16	0.79373167E 00	0.76984128E 00	0.74295343E 00	0.
17	0.12335275E 01	0.12335275E 01	0.18323024E 01	0.18934125E 01
17	0.14435633E 01	0.14698860E 01	0.15131271E 01	0.
18	0.12017673E 01	0.12017673E 01	0.13582474E 01	0.13659262E 01
18	0.12598716E 01	0.12989690E 01	0.13459794E 01	0.
19	0.35000000E 01	0.36500000E 01	0.10440000E 02	0.10710000E 02
19	0.35500000E 01	0.34800000E 01	0.34600000E 01	0.
20	0.15127879E 02	0.14989091E 02	0.14919697E 02	0.15055485E 02
20	0.15197273E 02	0.14989091E 02	0.15127879E 02	0.15023788E 02

21	0.98331211E	02	0.97429089E	02	0.96978028E	02	0.97880150E	02
21	0.98782271E	02	0.97429089E	02	0.98331211E	02	0.97654619E	02
22	0.		0.		0.		0.	
22	0.		0.		0.		0.	
23	0.		0.		0.		0.	
23	0.		0.		0.		0.	
24	0.		0.		0.		0.	
24	0.		0.		0.		0.40856759E	04
25	0.37713931E	03	0.37713931E	03	0.37713931E	03	0.37713931E	03
25	0.37530513E	03	0.37788212E	03	0.37208344E	03	0.	
26	0.10775409E	03	0.10332584E	03	0.36124454E	02	0.35213754E	02
26	0.10571975E	03	0.10858681E	03	0.10753856E	03	0.	
27	0.20987798E	00	0.20987798E	00	0.60557330E	00	0.63838077E	00
27	0.36711456E	00	0.38518487E	00	0.41417845E	00	0.	
28	0.22615211E	02	0.21685818E	02	0.21876005E	02	0.22479783E	02
28	0.38811261E	02	0.41825999E	02	0.44540156E	02	0.22215927E	02
29	0.		0.		0.		0.	
29	0.		0.		0.		-0.25581828E	-01
30	0.		0.		0.		0.	
30	0.		0.		0.		0.10008210E	01
31	0.		0.		0.		0.	
31	0.		0.		0.		0.21255385E	02
32	0.		0.		0.		0.	
32	0.		0.		0.		0.86842611E	02
33	0.		0.		0.		0.	
33	0.		0.		0.		0.25581828E	00
34	0.		0.		0.		0.	
34	0.		0.		0.		-0.77681380E	-02
35	0.		0.		0.		0.	
35	0.		0.		0.		0.88704950E	00
36	0.		0.		0.		0.	
36	0.		0.		0.		0.53198904E	04
37	0.		0.		0.		0.	
37	0.		0.		0.		0.88704950E	02
38	0.		0.		0.		0.	
38	0.		0.		0.		0.12733279E	00
39	0.		0.		0.		0.	
39	0.		0.		0.		0.11692308E	01
40	0.		0.		0.		0.	
40	0.		0.		0.		0.79203282E	03

41	0.	0.	0.	0.
41	0.86986095E 00	0.87063363E 00	0.86888189E 00	0.87041185E 00
42	0.	0.	0.	0.
42	0.31933862E 00	0.33535490E 00	0.35987215E 00	0.41866810E 03
43	0.	0.	0.	0.
43	0.16188000E 06	0.15868800E 06	0.15777600E 06	0.18630682E 09
44	0.12714253E 06	0.12191749E 06	0.42624410E 05	0.41549845E 05
44	0.14279513E 06	0.13597535E 06	0.12671167E 06	0.
45	0.45004411E-01	0.45004411E-01	0.16740640E 00	0.17304395E 00
45	0.91587909E-01	0.12303687E 00	0.15657382E 00	0.
46	0.57219744E 04	0.54868247E 04	0.71355990E 04	0.71899490E 04
46	0.13078307E 05	0.16729981E 05	0.19839729E 05	0.63835868E 04
47	0.81742492E 02	0.83133708E 02	0.83948224E 02	0.82643092E 02
47	0.11178040E 03	0.11781677E 03	0.12322813E 03	0.
48	0.46788746E 02	0.47585066E 02	0.48051289E 02	0.47304242E 02
48	0.63982205E 02	0.67437372E 02	0.70534792E 02	0.
49	0.32752122E 04	0.31406144E 04	0.40843596E 04	0.41154691E 04
49	0.74859181E 04	0.95761068E 04	0.11356101E 05	0.
50	0.	0.	0.	0.
50	0.21797179E 02	0.20912477E 02	0.19839729E 02	0.
51	0.	0.	0.	0.
51	0.	0.	0.	0.59479565E 04
52	0.	0.	0.	0.
52	0.	0.	0.	0.84282544E 03
53	0.	0.	0.	0.
53	0.	0.	0.	0.21244300E 02
54	0.	0.	0.	0.
54	0.	0.	0.	0.54158691E 04
55	0.	0.	0.	0.
55	0.	0.	0.	0.
56	0.	0.	0.	0.
56	0.	0.	0.	0.
57	0.	0.	0.	0.
57	0.	0.	0.	0.
58	0.	0.	0.	0.
58	0.	0.	0.	0.
59	0.	0.	0.	0.
59	0.	0.	0.	0.
60	0.	0.	0.	0.
60	0.	0.	0.	0.

SINGLE BREATH TECHNIQUE TO OBTAIN DIFFUSING CAPACITY OF LUNG FOR CO AND PULMONARY CAPILLARY BLOOD FLOW.

DATA OF JOHN SMITH PRINTED OUTPUT

BODY SURFACE AREA (BSA)

INSPIRED VOLUME STPD (VI STPD)

2715.6480 2730.3360 2714.8320

ALVEOLAR VOLUME STPD (VA STPD)

4030.9039 4053.1655 4162.3983

AVERAGE RESPIRING ALVEOLAR VOLUME STPD (VA STPD AVGE)

1315.2560 1322.8295 1447.5663

RESIDUAL VOLUME STPD (RV STPD NEON)

1591.4597 1600.6236 1751.5553

INITIAL CARBON MONOXIDE (CO O)

113.4845 113.4845 109.9381

INITIAL ACETYLENE (C2H2 O)

67.2990 67.2990 65.1959

ALVEOLAR / INITIAL CARBON MONOXIDE

0.8107 0.8107 0.5458

ALVEOLAR / INITIAL ACETYLENE

0.8321 0.8321 0.7362

BREATH HOLDING TIME

3.5000 3.6500 10.4400

ALVEOLAR OXYGEN CONCENTRATION (FO2)

15.1279 14.9891 14.9197

PARTIAL PRESSURE OF OXYGEN (PAO2)

98.3312 97.4291 96.9780

DIFFUSING CAPACITY OF THE LUNG FOR CARBON MONOXIDE (DLCO)

22.6152 21.6858 21.8760

BETA SLOPE OF CARBON MONOXIDE DISAPPEARANCE

ALPHA INTERCEPT OF CARBON MONOXIDE DISAPPEARANCE

BETA SLOPE OF ACETYLENE DISAPPEARANCE

ALPHA INTERCEPT OF ACETYLENE DISAPPEARANCE

TISSUE VOLUME OF THE LUNG (VT)

PULMONARY CAPILLARY BLOOD FLOW (Qc)

5721.9744 5486.8248 7135.5991

STROKE VOLUME (SV)

81.7425 83.1337 83.9482

STROKE INDEX (SI)

46.7887 47.5851 48.0513

CARDIAC INDEX (CI)

3275.2122 3140.6144 4084.3596

CARDIAC OUTPUT / WORK LOAD

0.0000 0.0000 0.0000

PREDICTED TOTAL LUNG CAPACITY (PTLC)

PREDICTED TISSUE VOLUME (PVT)

PREDICTED DIFFUSING CAPACITY (PDL CO)

PREDICTED CARDIAC OUTPUT (PCO)

TAKEN 5 APR 67

1.1471

4053.1655

15.023

11.5545

22.2157

-0.0255

1.0008

-0.0078

0.8877

792.0325

6383.5868

5947.9550

842.8257

21.2443

5415.8591

122

B29874